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                  SEL RN

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                  104495-35-4/BI OR 119951-66-5/BI OR 121563-65-3/BI OR
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                  14119-09-6/BI OR 14158-27-1/BI OR 14265-85-1/BI OR
                  14276-53-0/BI OR 14276-65-4/BI OR 14344-48-0/BI OR
                  14392-00-8/BI OR 14470-28-1/BI OR 14596-12-4/BI OR
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                  15128-03-7/BI OR 153-18-4/BI OR 15438-31-0/BI OR
                  15750-15-9/BI OR 15755-39-2/BI OR 15757-14-9/BI OR
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L21            1 SEA ABB=ON  PLU=ON  14344-48-0/RN
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L40              STRUCTURE
L41            5 SEA SSS SAM L40
L42          100 SEA SSS FUL L40
                 SAV L42 SCH919/A
L44              STRUCTURE
L45            1 SEA SUB=L42 SSS SAM L44
L46           20 SEA SUB=L42 SSS FUL L44

     FILE 'HCAPLUS' ENTERED AT 14:26:59 ON 11 JAN 2007
L47            6 SEA ABB=ON  PLU=ON  L46
L48            1 SEA ABB=ON  PLU=ON  L39

     FILE 'REGISTRY' ENTERED AT 15:52:22 ON 11 JAN 2007
L49            1 SEA ABB=ON  PLU=ON  84295-19-2/RN
L50           72 SEA ABB=ON  PLU=ON  C8 H16 N2 O4 S2/MF
L51            9 SEA ABB=ON  PLU=ON  L50 AND ?CYSTEINE?
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```
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L52          241 SEA ABB=ON  PLU=ON  L49 OR (N2S2 (2A) (LIGAND? OR
                 CHELAT?))
L53         1392 SEA ABB=ON  PLU=ON  L50 OR (?ETHYLENEDICYSTEINE? OR
                 ?ETHYLENE (A) DICYSTEINE?)
L54              QUE ABB=ON  PLU=ON  TARGET? (L) IMAG?
L55              QUE ABB=ON  PLU=ON  PET OR (POSITRON (2A) EMIS? (2A)
                 TOMOGRAPH?)
L56              QUE ABB=ON  PLU=ON  RADIONUCL? OR RADIO? (2A) NUCL? OR
                 TC OR TECHNETIUM
L57          161 SEA ABB=ON  PLU=ON  (L52 OR L53) AND L56
L58           23 SEA ABB=ON  PLU=ON  (L52 OR L53) AND L56 AND (L54 OR
                 L55)
L59            7 SEA ABB=ON  PLU=ON  L47 OR L48
L60           18 SEA ABB=ON  PLU=ON  L58 NOT L59

=> file reg
FILE 'REGISTRY' ENTERED AT 16:22:28 ON 11 JAN 2007
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STRUCTURE FILE UPDATES:   10 JAN 2007  HIGHEST RN 917201-58-2
DICTIONARY FILE UPDATES:  10 JAN 2007  HIGHEST RN 917201-58-2

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  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=> d l48 que stat
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L48           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L39


=> d l39 ide

L39  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2007 ACS on STN
RN   875544-24-4  REGISTRY
ED   Entered STN:  01 Mar 2006
CN   Propanamide, N-[4-(2-amino-1,6-dihydro-6-oxo-9H-purin-9-yl)-2-
     (hydroxymethyl)butyl]-2-[[2-[[(1R)-2-amino-1-(mercaptomethyl)-2-
     oxoethyl]amino]ethyl]amino]-3-mercapto-, (2R)- (9CI)  (CA INDEX
     NAME)
FS   STEREOSEARCH
MF   C18 H31 N9 O4 S2
SR   CA
LC   STN Files:   CA, CAPLUS, CASREACT

Absolute stereochemistry.
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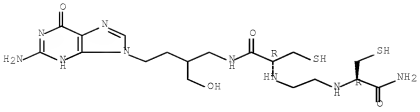

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file hcaplus
FILE 'HCAPLUS' ENTERED AT 16:23:18 ON 11 JAN 2007
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FILE COVERS 1907 - 11 Jan 2007 VOL 146 ISS 3
FILE LAST UPDATED: 10 Jan 2007 (20070110/ED)

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This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> d 148 ibib ed abs hitstr

L48 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:901688 HCAPLUS Full-text
DOCUMENT NUMBER: 144:219128
TITLE: 99mTc-Ethylenedicysteine-Guanine: Synthesis, Biodistribution, and Tumor Imaging in Animals
AUTHOR(S): Yang, David J.; Ozaki, Kaoru; Oh, Chang-Sok; Azhdarinia, Ali; Yang, Thomas; Ito, Megumi; Greenwell, Allison; Bryant, Jerry; Kohanim, Saady; Wong, Vincenzo K.; Kim, E. Edmund
CORPORATE SOURCE: Division of Diagnostic Imaging, The University of Texas MD Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE: Pharmaceutical Research (2005), 22(9), 1471-1479
CODEN: PHREEB; ISSN: 0724-8741
PUBLISHER: Springer Science+Business Media, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 144:219128
ED Entered STN: 26 Aug 2005

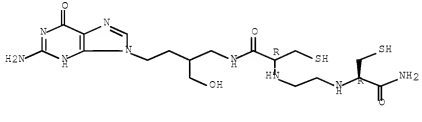
AB Purpose DNA markers are useful in assessing cell proliferation. The purpose of this study was to synthesize 99mTc-ethylenedicysteine- guanine (EC-Guan) for evaluation of cell proliferation. Methods Tumor cells were incubated with 99mTc-EC-Guan for cell cycle anal. Prostate tumor cells that were overexpressing the HSV thymidine kinase gene, or various tumor cells were incubated with 99mTc-EC-Guan at 0.5-2 h. Thymidine incorporation assays were performed in lung cancer cells incubated with EC-Guan at 0.1-1 mg/well. Tissue distribution, autoradiog., and planar scintigraphy of 99mTc-EC-Guan and 99mTc-EC (control) were determined in tumor-bearing rodents at 0.5-4 h. Results Cell culture assays indicated that EC-Guan was incorporated in DNA, and there was no significant uptake difference between HSVTK overexpressed and normal groups. Biodistribution and scintigraphic imaging studies of 99mTc-EC-Guan showed increased tumor/tissue count d. ratios as a function of time. Conclusions Our results indicate that 99mTc-EC-Guan may be useful as a tumor proliferation imaging agent.

IT 875544-24-4DP, technetium complexes 875544-24-4P
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); DGN (Diagnostic use); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(99mTc-ethylenedicysteine-guanine synthesis, biodistribution, and tumor imaging in animals)

RN 875544-24-4 HCAPLUS

CN Propanamide, N-[4-(2-amino-1,6-dihydro-6-oxo-9H-purin-9-yl)-2-(hydroxymethyl)butyl]-2-[[2-[[(1R)-2-amino-1-(mercaptomethyl)-2-oxoethyl]amino]ethyl]amino]-3-mercapto-, (2R)- (9CI) (CA INDEX NAME)

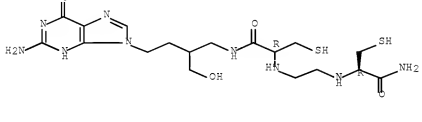
Absolute stereochemistry.



RN 875544-24-4 HCAPLUS

CN Propanamide, N-[4-(2-amino-1,6-dihydro-6-oxo-9H-purin-9-yl)-2-(hydroxymethyl)butyl]-2-[[2-[[(1R)-2-amino-1-(mercaptomethyl)-2-oxoethyl]amino]ethyl]amino]-3-mercapto-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> file reg
FILE 'REGISTRY' ENTERED AT 16:23:55 ON 11 JAN 2007

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provided by InfoChem.

STRUCTURE FILE UPDATES: 10 JAN 2007 HIGHEST RN 917201-58-2
DICTIONARY FILE UPDATES: 10 JAN 2007 HIGHEST RN 917201-58-2

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TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

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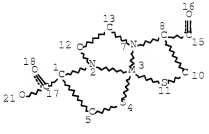
REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=> d l47 que stat
L40 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE
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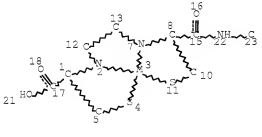

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L47           6 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L46


=> file hcaplus
FILE 'HCAPLUS' ENTERED AT 16:24:04 ON 11 JAN 2007
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FILE COVERS 1907 - 11 Jan 2007  VOL 146 ISS 3
FILE LAST UPDATED: 10 Jan 2007  (20070110/ED)

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 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d 147 1-6 ibib ed abs hitstr

L47  ANSWER 1 OF 6  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2006:617670  HCAPLUS  Full-text
DOCUMENT NUMBER:          145:110204
TITLE:                    Ethylenedicysteine-drug conjugates, compositions
                          and methods for tissue specific disease imaging
INVENTOR(S):              Yang, David J.; Liu, Chun W.; Yu, Dong-Fang;
                          Kim, E. Edmund
PATENT ASSIGNEE(S):       Board of Regents, University of Texas System,
                          USA
SOURCE:                   U.S., 125 pp., Cont.-in-part of U.S. Ser. No.
                          587,583.
                          CODEN: USXXAM
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   3
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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     US 7067111           B1    20060627    US 2000-599152
                                                                   200006
                                                                   21
     US 6692724           B1    20040217    US 1999-434313
                                                                   199910
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     WO 2001091807        A2    20011206    WO 2001-US18060
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WO 2001091807 A3 20020829
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1286704 A2 20030305 EP 2001-941895
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US 2000-587583 B2
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US 2000-599152 A
200006
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WO 2001-US18060 W
200106
01

ED Entered STN: 27 Jun 2006

AB The invention provides, in a general sense, a new labeling strategy employing 99mTc chelated with ethylenedicysteine (EC). EC is conjugated with a variety of tissue-targeting ligands and chelated to 99mTc for use as an imaging agent for tissue-specific diseases such as tumors, infections, hypoxia, myocardial infarction, apoptosis, Alzheimer's disease and endometriosis. The drug conjugates of the invention may also be used as a prognostic tool or as a tool to deliver therapeutics to specific sites within a mammalian body. Kits for use in tissue-specific disease imaging are also provided.

IT 224558-87-6P 378782-42-4P 660823-42-7P
660823-44-9DP, reaction products with glucosamine
660823-44-9P
RL: DGN (Diagnostic use); PKT (Pharmacokinetics); PRP (Properties);

SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(99mTc-ethylenedicysteine complex conjugated to tissue-targeting compds.)

RN 224558-87-6 HCAPLUS

CN Technetate(1-)-99Tc, [(2R,7R,16S)-16-[[4-[[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]amino]-2,7-bis[(mercapto-κS)methyl]-8,13-dioxo-3,6,9,12-tetraazaheptadecanedioato(4-)-κN3,κN6]oxo-, sodium, (SP-5-35)- (9CI) (CA INDEX NAME)

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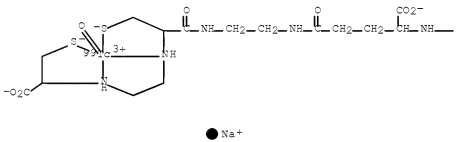

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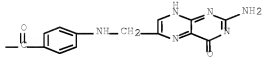

RN 378782-42-4 HCAPLUS

CN Technetate(1-)-99Tc, [(2R,7R,16S)-16-[[4-[[(2,4-diamino-6-pteridinyl)methyl]methylamino]benzoyl]amino]-2,7-bis[(mercapto-κS)methyl]-8,13-dioxo-3,6,9,12-tetraazaheptadecanedioato(4-)-κN3,κN6]oxo-, sodium, (SP-5-35)- (9CI) (CA INDEX NAME)

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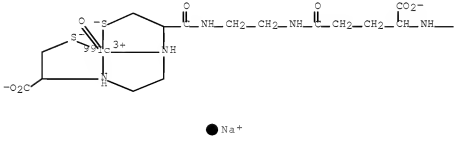

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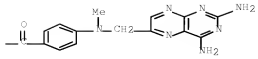

RN 660823-42-7 HCAPLUS
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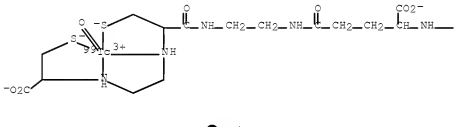
PAGE 1-A



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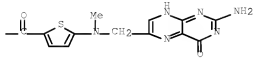

RN 660823-44-9 HCAPLUS
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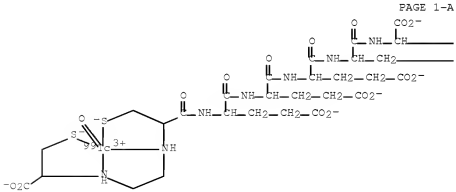
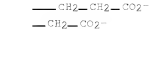
PAGE 1-A

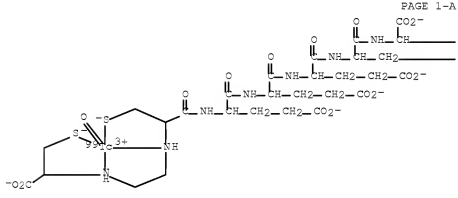


PAGE 1-B



RN 660823-44-9 HCAPLUS
CN Technetate(6-)-99Tc, [N-[2-[[(1R)-1-carboxy-2-(mercapto-κS)ethyl]amino-κN]ethyl]-L-cysteinyl-κN,κS-L-α-glutamyl-L-α-glutamyl-L-α-glutamyl-L-α-glutamyl-L-glutamato(9-)]-, hexasodium, (SP-5-35)- (9CI) (CA INDEX NAME)

PAGE 1-A



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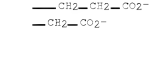


REFERENCE COUNT: 437 THERE ARE 437 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1021650 HCAPLUS Full-text
DOCUMENT NUMBER: 143:301456
TITLE: Metal radiolabeled PET imaging agents
INVENTOR(S): Chao, K. S. Clifford; Yang, David J.
PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA
SOURCE: PCT Int. Appl., 37 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005087275	A2	20050922	WO 2005-US7686	200503 09
WO 2005087275	A3	20060608		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GH, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-552244P P 200403 11
US 2004-552661P P 200403 11

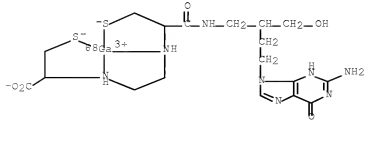
ED Entered STN: 22 Sep 2005

AB The invention relates to radiolabeled PET agents including a radioisotope, a chelator and a specific ligand. The radioisotope may include 60Cu, 62Cu, 61Cu, 64Cu and 68Ga. Generator-produced 68Ga radioisotopes may be used. Specific chelators include N2S2 moieties and N3S moieties. Specific ligands may include purine and pyrimidine bases, particularly adenine and guanine, a sugar-containing base, particularly glucosamine, galactosamine, or mannosamine, or a nitroimidazole analog, such as a 2-nitroimidazole or a 5-nitroimidazole, particularly metronidazole. Radiolabeled agents may be formed by first forming a chelator-ligand complex, which may be stored until it is needed, at which time the radioisotope may be added. Radiolabeled agents may be used in traditional PET imaging or in dynamic PET imaging.

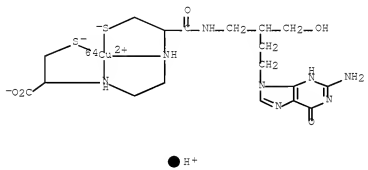
IT 864948-70-9
RL: DGN (Diagnostic use); PRT (Pharmacokinetics); BIOL (Biological study); USES (Uses)
(metal radiolabeled PET imaging agents)

RN 864948-70-9 HCAPLUS

CN Gallium-68Ga, [N-[2-[[(1R)-2-[[4-(2-amino-1,6-dihydro-6-oxo-9H-purin-9-yl)-2-(hydroxymethyl)butyl]amino]-1-[(mercapto-κS)methyl]-2-oxoethyl]amino-κN]ethyl]-L-cysteinato(3-)-κN,κS]-, (T-4)- (9CI) (CA INDEX NAME)



IT 864948-69-6P
RL: DGN (Diagnostic use); PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(metal radiolabeled PET imaging agents)
RN 864948-69-6 HCAPLUS
CN Cuprate(1-)-64Cu, [N-[2-[[(1R)-2-[[4-(2-amino-1,6-dihydro-6-oxo-9H-purin-9-yl)-2-(hydroxymethyl)butyl]amino]-1-[(mercapto-κS)methyl]-2-oxoethyl]amino-κN]ethyl]-L-cysteinato(3-)-κN,κS]-, hydrogen (9CI) (CA INDEX NAME)



● H+

L47 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:132235 HCAPLUS Full-text
DOCUMENT NUMBER: 140:195467
TITLE: Ethylenedicysteine-drug conjugates, compositions and methods for tissue specific disease imaging
INVENTOR(S): Yang, David J.; Liu, Chun W.; Yu, Dong-fang; Kim, E. Edmond
PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA
SOURCE: U.S., 58 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6692724	B1	20040217	US 1999-434313	19991025
US 7067111	B1	20060627	US 2000-599152	20000621
US 2005079133	A1	20050414	US 2003-672142	20030926
US 2005084448	A1	20050421	US 2003-672763	20030926
US 2006188438	A1	20060824	US 2006-405334	20060417
PRIORITY APPLN. INFO.:			US 1999-434313 A2	19991025

US 2000-587583 B2 200006 02

US 2000-599152 A1 200006 21

ED Entered STN: 18 Feb 2004

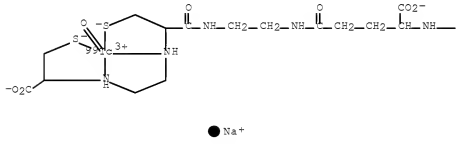
AB The invention provides, in a general sense, a new labeling strategy employing 99mTc chelated with ethylenedicysteine (EC). EC is conjugated with a variety of ligands and chelated to 99mTc for use as an imaging agent for tissue-specific diseases. The drug conjugates of the invention may also be used as a prognostic tool or as a tool to deliver therapeutics to specific sites within a mammalian body. The conjugated ligand is tissue specific and may be an anticancer agent or glutamate pentapeptide, or an agent targeting folate receptors, tumor apoptosis or tumor hypoxia. Kits for use in tissue-specific disease imaging are also provided. Synthesis, properties and tumor uptake studies of 99mTc-labeled EC conjugates with folate, metronidazole, nitroimidazole, pentaglutamate, annexin V, and colchicine are reported.

IT 224558-87-6P 378782-42-4P 660823-42-7P
660823-44-9P
RL: DGN (Diagnostic use); PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(ethylenedicysteine-conjugated technetium 99m complexes for tumor imaging)

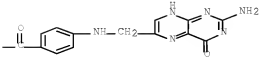
RN 224558-87-6 HCAPLUS

CN Technetate(1-)-99Tc, [(2R,7R,16S)-16-[[4-[[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]amino]-2,7-bis[(mercapto-κS)methyl]-8,13-dioxo-3,6,9,12-tetraazaheptadecanedioato(4-)-κN3,κN6]oxo-, sodium, (SP-5-35)- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

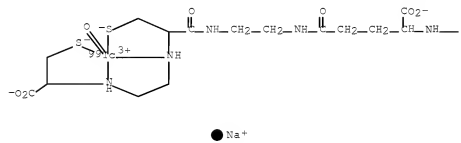


RN 378782-42-4 HCAPLUS

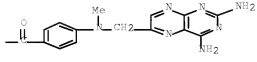
CN Technetate(1-)-99Tc, [(2R,7R,16S)-16-[[4-[[(2,4-diamino-6-pteridinyl)methyl]methylamino]benzoyl]amino]-2,7-bis[(mercapto-

κS)methyl]-8,13-dioxo-3,6,9,12-tetraazaheptadecanedioato(4-)-κN3,κN6]oxo-, sodium, (SP-5-35)- (9CI) (CA INDEX NAME)

PAGE 1-A



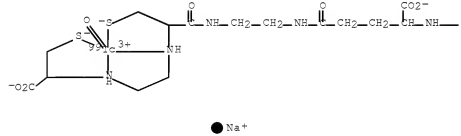
PAGE 1-B



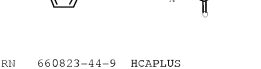
RN 660823-42-7 HCAPLUS

CN Technetate(1-)-99Tc, [(2R,7R,16S)-16-[[[5-[[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl]methylamino]-2-thienyl]carbonyl]amino]-2,7-bis[(mercapto-κS)methyl]-8-oxo-3,6,9,12-tetraazaheptadecanedioato(4-)-κN3,κN6]-, sodium, (SP-5-35)- (9CI) (CA INDEX NAME)

PAGE 1-A



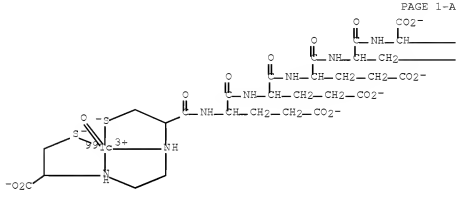
PAGE 1-B



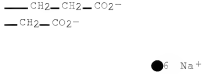
RN 660823-44-9 HCAPLUS

CN Technetate(6-)-99Tc, [N-[2-[[(1R)-1-carboxy-2-(mercapto-κS)ethyl]amino-κN]ethyl]-L-cysteinyl-κN,κS-L-α-glutamyl-L-α-glutamyl-L-α-glutamyl-L-α-glutamyl-L-glutamato(9-)]-, hexasodium, (SP-5-35)- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:476220 HCAPLUS Full-text
DOCUMENT NUMBER: 138:183138
TITLE: Preparation and preliminary evaluation of 99mTc-EC-For-MLFK
AUTHOR(S): Verbeke, K.; Verbeke, A.; Vanbilloen, H.; Verbruggen, A.
CORPORATE SOURCE: Laboratory of Radiopharmaceutical Chemistry, K.U. Leuven, Louvain, B-3000, Belg.
SOURCE: Nuclear Medicine and Biology (2002), 29(5), 585-592
CODEN: NMBIEO; ISSN: 0969-8051
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 25 Jun 2002
AB For-Met-Leu-Phe-Lys (For-MLFK), a chemotactic peptide that binds with high affinity to granulocytes and monocytes, was labeled with 99mTc using ethylene dicysteine (EC) as the metal chelating system. EC was selected because of the rapid renal excretion of its 99mTc-complex and therefore, was expected to enhance the degree of urinary elimination of the peptide-conjugate. 99mTc-EC-For-MLFK was prepared using a preformed chelate approach. After incubation of 99mTc-EC-For-MLFK with total blood, 68.1% of the labeled peptide was associated with WBC and 86% of this cell-associated activity was bound to granulocytes. Biodistribution studies in normal mice revealed a very fast blood

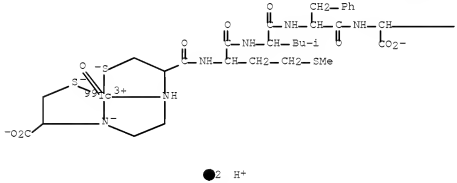
clearance (4.1% and 0.6% of I.D. in blood at resp. 5 and 60 min p.i.). However, elimination of the labeled peptide proceeds mainly via the hepatobiliary system (24.5% of I.D. in liver and 48.8% of I.D. in intestines at 60 min p.i.) and to a much lower degree via the kidneys (17.9% in renal system at 60 min p.i.). From these results, it is concluded that 99mTc-EC-For-MLFK is not suited to image infections, despite its high binding to granulocytes, since it leads to high, non-specific, abdominal activity.

IT 497947-68-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and preliminary evaluation of 99mTc-EC-For-MLFK)

RN 497947-68-9 HCAPLUS

CN Technetate(2-)-99Tc, [N-[2-[[(1S)-1-carboxy-2-(mercapto-κS)ethyl]amino-κN]ethyl]-D-cysteinyl-κN,κS-L-methionyl-L-leucyl-L-phenylalanyl-L-lysinato(5-)]-, dihydrogen, (SP-5-35)- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

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REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:885838 HCAPLUS Full-text
DOCUMENT NUMBER: 136:17356
TITLE: Ethylenedicysteine (ec)-drug conjugates, compositions and methods for tissue specific disease imaging
INVENTOR(S): Yang, David J.; Liu, Chun-wei; Yu, Dong-fang; Kim, E. Edmund
PATENT ASSIGNEE(S): Board of Regents The University of Texas System, USA
SOURCE: PCT Int. Appl., 176 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001091807	A2	20011206	WO 2001-US18060	200106

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WO 2001091807		A3	20020829		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
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EP 1286704		A2	20030305	EP 2001-941895	
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PRIORITY APPLN. INFO.:				US 2000-587583	A1
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					21
				US 1999-434313	A2
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				WO 2001-US18060	W
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ED Entered STN: 07 Dec 2001

AB The invention provides, in a general sense, a new labeling strategy employing 99mTc chelated with ethylenedicysteine (EC). EC is conjugated with a variety of ligands and chelated to 99mTc for use as an imaging agent for tissue-specific diseases. The drug conjugates of the invention may also be used as a prognostic tool or as a tool to deliver therapeutics to specific sites within a mammalian body. Kits for use in tissue-specific disease imaging are also provided.

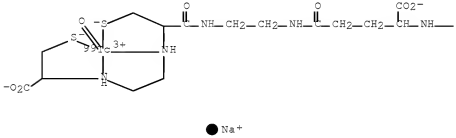
IT 224558-87-6P 378782-47-9P 378782-50-4P
378782-52-6P 378782-55-9P
RL: DGN (Diagnostic use); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of radiolabeled ethylenedicysteine-drug conjugates for tumor targeting)

RN 224558-87-6 HCAPLUS

CN Technetate(1-)-99Tc, [(2R,7R,16S)-16-[[4-[[(2-amino-1,4-dihydro-4-

oxo-6-pteridinyl)methyl]amino]benzoyl]amino]-2,7-bis[(mercapto-κS)methyl]-8,13-dioxo-3,6,9,12-tetraazaheptadecanedioato(4-)-κN3,κN6]oxo-, sodium, (SP-5-35)- (9CI) (CA INDEX NAME)

PAGE 1-A



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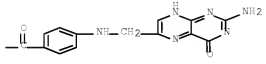
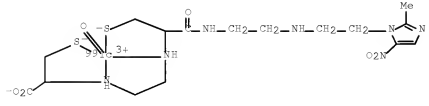


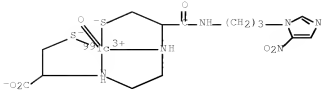
RN 378782-47-9 HCAPLUS

CN Technetium-99Tc, [N-[2-[[(1R)-1-[(mercapto-κS)methyl]-2-[[2-[[2-(2-methyl-5-nitro-1H-imidazol-1-yl)ethyl]amino]ethyl]amino]-2-oxoethyl]amino-κN]ethyl]-L-cysteinato(3-)-κN,κS]oxo-, (SP-5-35)- (9CI) (CA INDEX NAME)



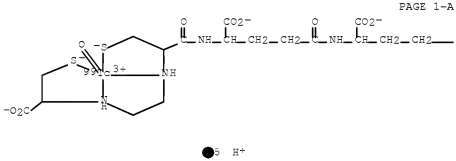
RN 378782-50-4 HCAPLUS

CN Technetium-99Tc, [N-[2-[[(1R)-1-[(mercapto-κS)methyl]-2-[[3-(5-nitro-1H-imidazol-1-yl)propyl]amino]-2-oxoethyl]amino-κN]ethyl]-L-cysteinato(3-)-κN,κS]oxo-, (SP-5-35)- (9CI) (CA INDEX NAME)

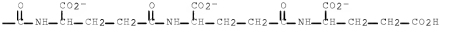


RN 378782-52-6 HCAPLUS
CN Technetate(5-)-99Tc, [N-[2-[[(1R)-1-carboxy-2-(mercapto-κS)ethyl]amino-κN]ethyl]-L-cysteinyl-κN,κS-L-γ-glutamyl-L-γ-glutamyl-L-γ-glutamyl-L-γ-glutamyl-L-glutamato(8-)]oxo-, pentahydrogen, (SP-5-35)- (9CI) (CA INDEX NAME)

PAGE 1-A

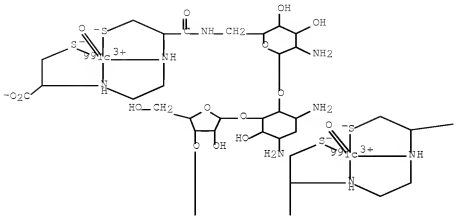


PAGE 1-B



RN 378782-55-9 HCAPLUS
CN Technetium-99Tc, [μ-[O-6-[[(2R)-2-[[2-[[(1R)-1-carboxy-2-(mercapto-κS)ethyl]amino-κN]ethyl]amino-κN]-3-(mercapto-κS)-1-oxopropyl]amino]-6-deoxy-β-L-idopyranosyl-(1→3)-O-β-D-ribofuranosyl-(1→5)-O-[2-amino-6-[[(2R)-2-[[2-[[(1R)-1-carboxy-2-(mercapto-κS)ethyl]amino-κN]ethyl]amino-κN]-3-(mercapto-κS)-1-oxopropyl]amino]-2,6-dideoxy-α-D-glucopyranosyl-(1→4)]-2-deoxy-D-streptaminato(6-)]]dioxodi-, stereoisomer (9CI) (CA INDEX NAME)

PAGE 1-A



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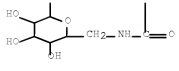
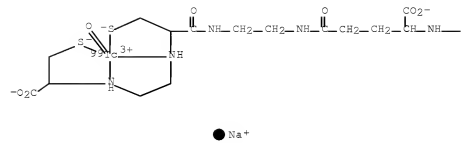


IT 378782-42-4 378782-44-6
RL: DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(preparation of radiolabeled ethylenedicysteine-drug conjugates for tumor targeting)

RN 378782-42-4 HCAPLUS

CN Technetate(1-)-99Tc, [(2R,7R,16S)-16-[[4-[[(2,4-diamino-6-pteridinyl)methyl]methylamino]benzoyl]amino]-2,7-bis[(mercapto-κS)methyl]-8,13-dioxo-3,6,9,12-tetraazaheptadecanedioato(4-)-κN3,κN6]oxo-, sodium, (SP-5-35)- (9CI) (CA INDEX NAME)

PAGE 1-A



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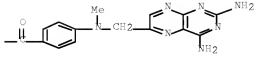
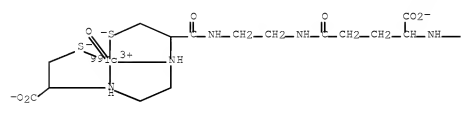


RN 378782-44-6 HCAPLUS
CN Technetate(1-)-99Tc, [(2R,7R,16S)-16-[[[5-[[(1,4-dihydro-2-methyl-4-oxo-6-quinazolinyl)methyl]methylamino]-2-thienyl]carbonyl]amino]-2,7-bis[(mercapto-κS)methyl]-8,13-dioxo-3,6,9,12-tetraazaheptadecanedioato(4-)-κN3,κN6]oxo-, sodium, (SP-5-35)- (9CI) (CA INDEX NAME)

PAGE 1-A



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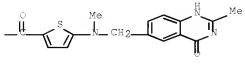


L47 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:125562 HCAPLUS Full-text
DOCUMENT NUMBER: 130:334722
TITLE: 99mTc-ethylenedicysteine-folate: A new tumor

	imaging agent. Synthesis, labeling and evaluation in animals
AUTHOR(S):	Ilgan, Seyfettin; Yang, David J.; Higuchi, Tetsuya; Zareneyrizi, Fereshteh; Bayhan, Hikmet; Yu, Dongfang; Kim, E. Edmund; Podoloff, Donald A.
CORPORATE SOURCE:	Department of Nuclear Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE:	Cancer Biotherapy & Radiopharmaceuticals (1998), 13(6), 427-435 CODEN: CBRAFJ; ISSN: 1084-9785
PUBLISHER:	Mary Ann Liebert, Inc.
DOCUMENT TYPE:	Journal
LANGUAGE:	English

ED Entered STN: 25 Feb 1999

AB It is known that membrane folic acid receptors are responsible for cellular accumulation of folate and folate analogs such as methotrexate and overexpressed on various tumor cells. However, these receptors are highly restricted in normal differentiated tissues. Results of limited in vitro and in vivo animal studies suggest that folate receptors could be a potential target for tumor imaging. This study aimed to develop a 99mTc-labeled folic acid using ethylenedicysteine (EC) as a chelator and evaluate its labeling efficiency and potential use as a tumor seeking agent. Tissue distribution of 99mTc-EC-folate was determined in breast tumor-bearing rats at 20 min, 1, 2, and 4 h (n=3/time interval, 370 KBq/rat, i.v.). Blocking study was employed to determine receptor-mediated process; 99mTc-EC-folate was co-administrated with 50 and 150 μmol/kg of cold folic acid to tumor-bearing rats. Planar imaging and whole-body autoradiograms were performed. The data was compared to that using 99mTc-EC (control). In animal studies, tumor/blood count d. ratios at 20 min-4 h increased from 0.81±0.09 to 1.23±0.13 with 99mTc-EC-folate. Conversely, these values showed time-dependent decrease from 0.77±0.32 to 0.65±0.01 with 99mTc-EC in the same time period. Tumor/muscle and tumor/blood count d. ratios significantly decreased with folic acid co-administrations. Planar images and autoradiograms confirmed that the tumors could be visualized clearly with 99mTc-EC-folate.

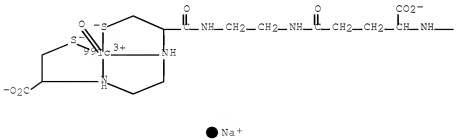
IT 224558-87-6P

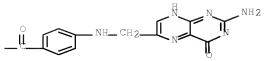
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(synthesis of, biodistribution of and tumor imaging with 99mTc-ethylenedicysteine-folate)

RN 224558-87-6 HCAPLUS

CN Technetate(1-)-99Tc, [(2R,7R,16S)-16-[[4-[[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]amino]-2,7-bis[(mercapto-κS)methyl]-8,13-dioxo-3,6,9,12-tetraazaheptadecanedioato(4-)-κN3,κN16]oxo-, sodium, (SP-5-35)- (9CI) (CA INDEX NAME)

PAGE 1-A





REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FILE LAST UPDATED: 10 Jan 2007 (20070110/ED)

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=> d l60 que stat
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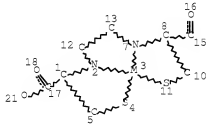
L40 STR



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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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NUMBER OF NODES IS 16

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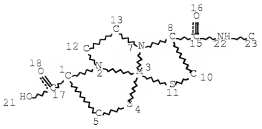

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STEREO ATTRIBUTES: NONE
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L49            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  84295-19-2/RN
L50           72 SEA FILE=REGISTRY ABB=ON  PLU=ON  C8 H16 N2 O4 S2/MF
L52          241 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 OR (N2S2 (2A)
                 (LIGAND? OR CHELAT?))
L53         1392 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L50 OR (?ETHYLENEDICYSTE
                 INE? OR ?ETHYLENE (A) DICYSTEINE?)
L54              QUE  ABB=ON  PLU=ON  TARGET? (L) IMAG?
L55              QUE  ABB=ON  PLU=ON  PET OR (POSITRON (2A) EMIS? (2A) TOM
                 OGRAPH?)
L56              QUE  ABB=ON  PLU=ON  RADIONUCL? OR RADIO? (2A) NUCL? OR T
                 C OR TECHNETIUM
L58           23 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L52 OR L53) AND L56
                 AND (L54 OR L55)
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=> d l60 1-18 ibib ed abs hitind

L60  ANSWER 1 OF 18  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2006:1048518  HCAPLUS  Full-text
DOCUMENT NUMBER:          146:41024
TITLE:                    A novel 99mTc-labeled testosterone derivative as
                          a potential agent for targeting androgen
                          receptors
AUTHOR(S):                Das, Tapas; Banerjee, Sharmila; Samuel, Grace;
                          Bapat, Ketaki; Subramanian, Suresh; Pillai,
                          Maroor R. A.; Venkatesh, Meera
CORPORATE SOURCE:         Radiopharmaceuticals Division, Bhabha Atomic
                          Research Centre, Mumbai, 400085, India
SOURCE:                   Bioorganic & Medicinal Chemistry Letters (2006),
                          16(22), 5788-5792
                          CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER:                Elsevier Ltd.
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
ED   Entered STN:  09 Oct 2006
AB   With an insight that ligands possessing a N2S2 tetradentate array of donor atoms serve
     as ideal bifunctional chelating agents (BFCA) in the radiolabeling of target-specific
     agents, 5-hydroxy-3,7-diazanonan-1,9-dithiol (DAHPES) with a derivatizable substituent
     in the form of a hydroxyl group in the backbone was synthesized.  The preparation of a
     steroid conjugate via coupling of this BFCA with testosterone-3-(O-carboxymethyl) oxime
     and the subsequent radiolabeling of the conjugate under optimized conditions with
     99mTc, the ideal diagnostic radionuclide in nuclear medicine procedures, are reported.
     The immunoreactivity of the radiolabeled conjugate was demonstrated in a study using
     anti-testosterone antibodies, wherein the radiolabeled conjugate exhibited significant
     binding with antiserum to testosterone.  Cell-uptake studies in DU145 prostate
     carcinoma cell line bearing androgen receptors (ARs) and comparison with AR non-bearing
     breast carcinoma cell line revealed the specific binding of the steroidal moiety with
     the testosterone receptor.
CC   8-9 (Radiation Biochemistry)
ST   technetium testosterone deriv androgen receptor prostate
     carcinoma imaging
IT   Imaging agents
        (contrast; 99mTc-labeled testosterone derivative as for potential
        targeting androgen receptors)
IT   Imaging
        (tumor; 99mTc-labeled testosterone derivative as for potential
        targeting androgen receptors)
IT   916445-04-0DP, Tc-99m labeled
     RL: DGN (Diagnostic use); PKT (Pharmacokinetics); SPN (Synthetic
     preparation); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (99mTc-labeled testosterone derivative as for potential targeting
        androgen receptors)

L60  ANSWER 2 OF 18  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2006:681452  HCAPLUS  Full-text
DOCUMENT NUMBER:          145:130695
TITLE:                    Conjugates for dual imaging and
                          radiochemotherapy: composition, manufacturing,
                          and applications
INVENTOR(S):              Yang, David J.; Yu, Dongfang; Chanda, Mithu;
                          Azhdarinia, Ali; Oh, Changsok; Kim, E. Edward
PATENT ASSIGNEE(S):       Board of Regents, The University of Texas
                          System, USA
SOURCE:                   PCT Int. Appl., 72 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.        DATE
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WO 2006074272	A2	20060713	WO 2006-US269	200601 05
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2006182687	A1	20060817	US 2006-326117	200601 05
PRIORITY APPLN. INFO.:			US 2005-641559P P	200501 05

ED Entered STN: 14 Jul 2006

AB Compns. and methods for dual imaging and for dual chemotherapy and radiotherapy are disclosed. More particularly, the invention concerns compds. comprising the structure X1-Y-X2, wherein Y comprises two or more carbohydrate residues covalently attached to one another, X1 and X2 are diagnostic or therapeutic moieties covalently attached to Y, provided that when Y does not comprise a glucosamine residue, X1 and X2 are diagnostic moieties. Conjugates consisting of a carbohydrate backbone to which diagnostic and/or therapeutic moieties are attached are used as tumor- targeting agents with dual diagnostic (such as MRI + PET) and dual therapeutic (chemotherapy + radiotherapy) capabilities. The present invention also concerns methods of synthesis of these conjugates, application of such compds. for dual imaging and treatment of hyperproliferative disease, and kits for preparing a radiolabeled therapeutic or diagnostic compound

IC ICM A61K

CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1, 8, 9

ST tumor targeting carbohydrate imaging therapeutic agent conjugate

IT Angiogenesis inhibitors
Antimicrobial agents
Antitumor agents
Apoptosis
Chemotherapy
Diagnosis
Drug delivery systems
Gene therapy
Human
Hypoxia
Imaging agents
Immunotherapy
Leukemia
Lymphoma
Neoplasm
Positron-emission tomography
Radiotherapy
Scintigraphic agents
Scintigraphy
Single-photon-emission computed tomography
(conjugates for dual imaging and radiochemotherapy)

IT Amines, biological studies
Radionuclides, biological studies
Thiols, biological studies
RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological

study); USES (Uses)
(conjugates for dual imaging and radiochemotherapy)
IT 59-05-2DP, Methotrexate, conjugates 117-96-4DP, Diatrizoate, conjugates 3416-24-8DP, Glucosamine, conjugates 9012-76-4DP, Chitosan, conjugates 15757-14-9DP, Gallium 68, complexes with oligosaccharide conjugates, biological studies 378784-45-3DP, Technetium 99m, complexes with oligosaccharide conjugates, biological studies
RL: DGN (Diagnostic use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(conjugates for dual imaging and radiochemotherapy)
IT 59-05-2D, Methotrexate, reaction product with polyglucosamine 60-00-4D, Edta, radiolabeled oligosaccharide conjugates, biological studies 67-43-6D, Dtpa, radiolabeled oligosaccharide conjugates 117-96-4D, reaction product with polyglucosamine 1398-61-4, Chitin 1429-50-1D, Edtmp, radiolabeled oligosaccharide conjugates 2418-14-6D, DMSA, radiolabeled oligosaccharide conjugates 2809-21-4D, Hedp, radiolabeled oligosaccharide conjugates 9005-49-6, Heparin, biological studies 9012-76-4, Chitosan 10098-91-6, 90y, biological studies 13967-65-2, 166Ho, biological studies 13982-06-4, Copper 60, biological studies 14119-09-6, 67Ga, biological studies 14158-27-1, 89Sr, biological studies 14276-53-0, Copper 62, biological studies 14304-48-0D, reaction product with polyglucosamine 14378-26-8, 188Re, biological studies 14391-32-3, 157Gd, biological studies 14913-49-6, 212Bi, biological studies 14998-63-1, 186Re, biological studies 15064-65-0, 201Tl, biological studies 15128-03-7, Copper 61, biological studies 15750-15-9, Indium 111, biological studies 15755-33-6, 72As, biological studies 15757-86-5, Copper 67, biological studies 15766-00-4, 153Sm, biological studies 15776-20-2, 213Bi, biological studies 15827-60-8D, Dtpmp, radiolabeled oligosaccharide conjugates 35110-26-0, Polyglucosamine 35110-26-0D, reaction products with 60239-18-1D, Dota, radiolabeled oligosaccharide conjugates 60239-20-5D, Trita, radiolabeled oligosaccharide conjugates 60239-22-7D, Teta, radiolabeled oligosaccharide conjugates 66516-09-4D, Mag3, radiolabeled oligosaccharide conjugates 89156-33-2D, radiolabeled oligosaccharide conjugates 91987-74-5D, radiolabeled oligosaccharide conjugates 113786-33-7D, Bopta, radiolabeled oligosaccharide conjugates 120041-08-9D, radiolabeled oligosaccharide conjugates 120041-09-0D, radiolabeled oligosaccharide conjugates 132446-35-6D, DOTMP, radiolabeled oligosaccharide conjugates 133081-24-0D, 6-Hydrazinonicotinic acid, radiolabeled oligosaccharide conjugates 136705-18-5D, DOTEP, radiolabeled oligosaccharide conjugates 138149-64-1D, DOTPP, radiolabeled oligosaccharide conjugates 145089-54-9D, radiolabeled oligosaccharide conjugates 161167-43-7D, DOTPME, radiolabeled oligosaccharide conjugates 175985-20-3D, radiolabeled oligosaccharide conjugates 182132-19-0D, radiolabeled oligosaccharide conjugates
RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates for dual imaging and radiochemotherapy)

L60 ANSWER 3 OF 18 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:338143 HCAPLUS Full-text
DOCUMENT NUMBER: 144:381973
TITLE: Compositions for detecting hyaluronidase activity in situ and methods of utilizing same
INVENTOR(S): Neeman, Michal; Shiftan, Liora
PATENT ASSIGNEE(S): Israel
SOURCE: U.S. Pat. Appl. Publ., 20 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006078500	A1	20060413	US 2004-959417	20041007
PRIORITY APPLN. INFO.:			US 2004-959417	20041007

ED Entered STN: 13 Apr 2006
AB A composition-of-matter is provided. The composition-of-matter comprising a chelator moiety-hyaluronan complex bound to a solid support. Also provided are methods of in-situ assessing hyaluronidase activity using such compns.
INCL 424009340; 435020000; 536053000
CC 1-6 (Pharmacology)
Section cross-reference(s): 63, 64
IT Antitumor agents
Human
Imaging
Positron-emission tomography
Radiography
X-ray
(compns. for detecting hyaluronidase activity in situ and methods of utilizing same)
IT 7429-91-6, Dysprosium, biological studies 7439-91-0, Lanthanum, biological studies 7439-96-5, Manganese, biological studies 7440-26-8, Technetium, biological studies 7440-47-3, Chromium, biological studies 7440-53-1, Europium, biological studies 7440-54-2, Gadolinium, biological studies 7440-58-6, Hafnium, biological studies 7440-60-0, Holmium, biological studies 7440-64-4, Ytterbium, biological studies 7440-74-6, Indium, biological studies
RL: DGN (Diagnostic use); PEP (Physical, engineering or chemical process); PYP (Physical process); BIOL (Biological study); PROC (Process); USES (Uses)
(compns. for detecting hyaluronidase activity in situ and methods of utilizing same)
IT 58-85-5, Biotin 60-00-4, Ethylenediaminetetraacetic acid, processes 67-42-5, Ethylenebis(oxyethylenenitrilo)tetraacetic acid 67-43-6, Diethylenetriaminepentaacetic acid 139-13-9, Nitrilotriacetic acid 150-39-0, N-(Hydroxyethyl)ethylenediaminetri acetic acid 482-54-2, 1,2-Diaminocyclohexane-N,N,N',N'-tetraacetic acid 869-52-3 14344-48-0 22907-28-4 56491-86-2 60239-18-1, 1,4,7,10-Tetraazacyclododecane-N,N',N'',N'''-tetraacetic acid 60239-22-7, 1,4,8,11-Tetraazacyclotetradecane-N,N',N'',N'''-tetraacetic acid 114873-37-9 115416-38-1 120041-08-9
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process)
(compns. for detecting hyaluronidase activity in situ and methods of utilizing same)

L60 ANSWER 4 OF 18 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2006:310062 HCAPLUS Full-text
DOCUMENT NUMBER:	144:447150
TITLE:	Targeted molecular imaging in oncology
AUTHOR(S):	Yang, David J.; Kim, E. Edmund; Inoue, Tomio
CORPORATE SOURCE:	Department of Experimental Diagnostic Imaging, The University of Texas M.D. Anderson Cancer Center, Houston, TX, USA
SOURCE:	Annals of Nuclear Medicine (2006), 20(1), 1-11 CODEN: ANMEEX; ISSN: 0914-7187
PUBLISHER:	Japanese Society of Nuclear Medicine
DOCUMENT TYPE:	Journal; General Review

LANGUAGE: English
ED Entered STN: 04 Apr 2006
AB A review. Improvement of scintigraphic tumor imaging is extensively determined by the development of more tumor specific radiopharmaceuticals. Thus, to improve the differential diagnosis, prognosis, planning and monitoring of cancer treatment, several functional pharmaceuticals have been developed. Application of mol. targets for cancer imaging, therapy and prevention using generator-produced isotopes is the major focus of ongoing research projects. Radionuclide imaging modalities (positron emission tomog., PET; single photon emission computed tomog., SPECT) are diagnostic cross-sectional imaging techniques that map the location and concentration of radionuclide-labeled radiotracers. 99mTc- and 68Ga-labeled agents using ethylenedicysteine (EC) as a chelator were synthesized and their potential uses to assess tumor targets were evaluated. 99mTc (t1/2 = 6 h, 140 keV) is used for SPECT and 68Ga (t1/2 = 68 min, 511 keV) for PET. Mol. targets labeled with Tc-99m and Ga-68 can be utilized for prediction of therapeutic response, monitoring tumor response to treatment and differential diagnosis. Mol. targets for oncol. research in (1) cell apoptosis, (2) gene and nucleic acid-based approach, (3) angiogenesis (4) tumor hypoxia, and (5) metabolic imaging are discussed. Numerous imaging ligands in these categories have been developed and evaluated in animals and humans. Mol. targets were imaged and their potential to redirect optimal cancer diagnosis and therapeutics were demonstrated.
CC 8-0 (Radiation Biochemistry)
ST review targeted mol imaging oncol cancer
IT Gene, animal
Nucleic acids
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(as mol. targets; targeted mol. imaging in oncol.)
IT Diagnosis
(cancer; targeted mol. imaging in oncol.)
IT Imaging agents
(contrast; targeted mol. imaging in oncol.)
IT Angiogenesis
Apoptosis
Hypoxia
Metabolism
(mol. targets in; targeted mol. imaging in oncol.)
IT Imaging
(mol.; targeted mol. imaging in oncol.)
IT Medicine
(oncol.; targeted mol. imaging in oncol.)
IT Diagnosis
(radiodiagnosis; targeted mol. imaging in oncol.)
IT Drug targets
Human
Neoplasm
Positron-emission tomography
Single-photon-emission computed tomography
(targeted mol. imaging in oncol.)
IT Radionuclides, biological studies
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(targeted mol. imaging in oncol.)
IT Imaging
(tumor; targeted mol. imaging in oncol.)
REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L60 ANSWER 5 OF 18 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:175476 HCAPLUS Full-text
DOCUMENT NUMBER: 145:485062
TITLE: Biodistribution of 99Tcm labeled ethylenedicysteine-deoxyglucose in mice
AUTHOR(S): Tang, Jun; Zhou, Jundong; Chen, Jie; Yang, Yi
CORPORATE SOURCE: The Second Affiliated Hospital, Suzhou University, Suzhou, 215004, Peop. Rep. China

SOURCE: Zhonghua Heyixue Zazhi (2005), 25(3), 179-181
CODEN: CITCDE; ISSN: 0253-9780
PUBLISHER: Jiangsusheng Yuanzi Yixue Yanjiuso
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
ED Entered STN: 27 Feb 2006
AB The biodistributions of 99Tcm labeled ethylenedicysteine -deoxyglucose (EC-DG) in normal mice and S180 sarcoma bearing mice were evaluated. The percentage injected dose per g (%ID/g) of 99Tcm-EC-DG in the organs and tissues including heart, kidney, lung and muscle of the normal mice were calculated Meanwhile, the radioactivity ratios of target to background (T/NT) of tumor to blood, muscle, lung and liver of S180 sarcoma bearing mice were also calculated, resp. The results showed that %ID/g in kidney was significantly higher than those in other organs, and 99Tcm-EC-DG was not uptaken in brain. The %ID/g decreased rapidly in 1 h of all selected organs except blood. T/NT value of tumor to blood, muscle and lung gradually increased after the injection of 99Tcm-EC-DG, and all reached above 1.0 at the 4th h. The imaging showed that the radioactivity of the tissues surrounding the tumor decreased gradually after the injection, and the tumor site was clearly visualized at the 4th h. 99Tcm-EC-DG could be used as an imaging agent for glucose metabolism of tumor.
CC 8-9 (Radiation Biochemistry)
Section cross-reference(s): 63
ST technetium radioisotope ethylenedicysteine
deoxyglucose sarcoma imaging biodistribution pharmacokinetics
IT Blood
Imaging agents
Kidney
Liver
Lung
Muscle
Sarcoma
Stomach
Tomography
(biodistribution of 99Tcm labeled ethylenedicysteine
-deoxyglucose in mice)
IT Biological transport
(uptake; biodistribution of 99Tcm labeled
ethylenedicysteine-deoxyglucose in mice)
IT 14133-76-7DP, Technetium 99, ethylenedicysteine
-glucosamine complex with, biological studies 378230-75-2DP,
complex with Tc-99m
RL: DGN (Diagnostic use); PKT (Pharmacokinetics); SPN (Synthetic
preparation); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(biodistribution of 99Tcm labeled ethylenedicysteine
-deoxyglucose in mice)
IT 378784-45-3, 99Tcm, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(biodistribution of 99Tcm labeled ethylenedicysteine
-deoxyglucose in mice)

L60 ANSWER 6 OF 18 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:524970 HCAPLUS Full-text
DOCUMENT NUMBER: 143:48042
TITLE: N2S2 chelate-targeting
ligand conjugates
INVENTOR(S): Yang, David J.; Yu, Dong-fang; Oh, Chang-Sok;
Bryant, Jerry L.
PATENT ASSIGNEE(S): Board of Regents, the University of Texas
System, USA; Cell Point LLC
SOURCE: U.S. Pat. Appl. Publ., 68 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 2005129619	A1	20050616	US 2003-732919	200312 10
PRIORITY APPLN. INFO.:			US 2003-732919	200312 10

OTHER SOURCE(S): MARPAT 143:48042
ED Entered STN: 17 Jun 2005
AB The invention provides, in a general sense, a new labeling strategy employing compds. that are N2S2 chelates conjugated to a targeting ligand, wherein the targeting ligand is a disease cell cycle targeting compound, a tumor angiogenesis targeting ligand, a tumor apoptosis targeting ligand, a disease receptor targeting ligand, amifostine, angiostatin, monoclonal antibody C225, monoclonal antibody CD31, monoclonal antibody CD40, capecitabine, a COX-2 inhibitor, deoxycytidine, fullerene, herceptin, human serum albumin, lactose, leuteinizing hormone, pyridoxal, quinazoline, thalidomide, transferrin, or tri-Me lysine. The present invention also pertains to kits employing the compds. of interest, and methods of assessing the pharmacol. of an agent of interest using the present compds.
IC ICM A61K0049-00
ICS A61K0051-00; C07K0016-46; C07F0005-00
INCL 424009340; 424009360; 530391100; 530400000; 534016000
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 8
ST antibody drug conjugate targeted radionuclide tumor imaging agent
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Bad; targeted radiolabeled ligands for tumor imaging and therapy)
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Bak; targeted radiolabeled ligands for tumor imaging and therapy)
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Bax; targeted radiolabeled ligands for tumor imaging and therapy)
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Bcl-2; targeted radiolabeled ligands for tumor imaging and therapy)
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Bcl-xL; targeted radiolabeled ligands for tumor imaging and therapy)
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Bid; targeted radiolabeled ligands for tumor imaging and therapy)
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(TRAIL (tumor necrosis factor-related apoptosis-inducing ligand); targeted radiolabeled ligands for tumor imaging and therapy)
IT Tocopherols
RL: NUU (Other use, unclassified); USES (Uses)
(antioxidant; targeted radiolabeled ligands for tumor imaging and therapy)
IT Neoplasm
Neoplasm
(head and neck; targeted radiolabeled ligands for tumor imaging and therapy)
IT Drug delivery systems
(immunoconjugates; targeted radiolabeled ligands for

tumor imaging and therapy)
IT Drug delivery systems
(immunotoxins; targeted radiolabeled ligands for tumor imaging and therapy)
IT Antibodies and Immunoglobulins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(monoclonal, conjugates, radiolabeled; targeted radiolabeled ligands for tumor imaging and therapy)
IT Androgens
Estrogens
Peptides, biological studies
Transferrins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(radiolabeled conjugates; targeted radiolabeled ligands for tumor imaging and therapy)
IT Uterus, neoplasm
(sarcoma; targeted radiolabeled ligands for tumor imaging and therapy)
IT Albumins, biological studies
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(serum, radiolabeled conjugates; targeted radiolabeled ligands for tumor imaging and therapy)
IT Angiogenesis
Antioxidants
Apoptosis
Chelating agents
Chromatin
Head and Neck, neoplasm
Head and Neck, neoplasm
Human
Imaging agents
Neoplasm
Ovary, neoplasm
Scintigraphic agents
Scintigraphy
Test kits
(targeted radiolabeled ligands for tumor imaging and therapy)
IT Epidermal growth factor receptors
Gonadotropin receptors
Gonadotropin-releasing hormone receptor
Lipid metabolism
Transferrin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(targeted radiolabeled ligands for tumor imaging and therapy)
IT Sarcoma
(uterine; targeted radiolabeled ligands for tumor imaging and therapy)
IT Reproductive system
(vulva, neoplasm; targeted radiolabeled ligands for tumor imaging and therapy)
IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(αvβ3; targeted radiolabeled ligands for tumor imaging and therapy)
IT 50-81-7, Vitamin c, uses 59-43-8, Thiamine, uses 65-23-6, Pyridoxine 153-18-4, Rutin
RL: NUU (Other use, unclassified); USES (Uses)
(antioxidant; targeted radiolabeled ligands for tumor imaging and therapy)
IT 50-99-7, Glucose, biological studies 3416-24-8, Glucosamine
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(metabolism; targeted radiolabeled ligands for tumor imaging and therapy)
IT 603-35-0, Triphenylphosphine, uses 7772-99-8, Stannous chloride,

uses 14844-07-6, Dithionite 15438-31-0, Ferrous ion, uses 22541-90-8, Stannous ion, uses
RL: NUU (Other use, unclassified); USES (Uses)
(reducing agent; targeted radiolabeled ligands for tumor imaging and therapy)

IT 80449-01-0, Topoisomerase 169592-56-7, Caspase 3 329900-75-6, Cox-2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(targeted radiolabeled ligands for tumor imaging and therapy)

IT 50-35-1D, Thalidomide, radiolabeled conjugates 56-84-8D, Aspartic acid, radiolabeled conjugates 56-86-0D, Glutamic acid, radiolabeled conjugates 56-87-1D, Lysine, radiolabeled conjugates 57-83-0D, Progestin, radiolabeled conjugates, biological studies 58-61-7D, Adenosine, radiolabeled conjugates, biological studies 63-42-3D, Lactose, radiolabeled conjugates 66-72-8D, Pyridoxal, radiolabeled conjugates 73-40-5D, Guanine, radiolabeled conjugates 107-15-3D, Ethylenediamine, radiolabeled conjugates 253-82-7D, Quinazoline, radiolabeled conjugates 541-15-1D, Carnitine, radiolabeled conjugates 927-68-4D, radiolabeled conjugates 951-77-9D, Deoxycytidine, radiolabeled conjugates 951-77-9D, Deoxycytidine, reaction product with ethylenedicysteine 9002-67-9D, LH, radiolabeled conjugates 9034-40-6D, LHRH, radiolabeled conjugates 10098-91-6D, Yttrium 90, conjugated complexes, biological studies 13967-65-2D, Holmium 166, conjugated complexes, biological studies 13981-25-4D, Copper 64, conjugated complexes, biological studies 13982-06-4D, Copper 60, conjugated complexes, biological studies 14119-09-6D, Gallium 67, conjugated complexes, biological studies 14158-27-1D, Strontium 89, conjugated complexes, biological studies 14265-85-1D, Actinium 225, conjugated complexes, biological studies 14276-53-0D, Copper 62, conjugated complexes, biological studies 14276-65-4D, Gadolinium 153, conjugated complexes, biological studies 14378-26-8D, Rhenium 188, conjugated complexes, biological studies 14392-00-8D, Titanium 45, conjugated complexes, biological studies 14596-12-4D, Iron 59, conjugated complexes, biological studies 14913-49-6D, Bismuth 212, conjugated complexes, biological studies 14998-63-1D, Rhenium 186, conjugated complexes, biological studies 15128-03-7D, Copper 61, conjugated complexes, biological studies 15750-15-9D, Indium 111, conjugated complexes, biological studies 15755-39-2D, Astatine 211, conjugated complexes, biological studies 15757-14-9D, Gallium 68, conjugated complexes, biological studies 15757-86-5D, Copper 67, conjugated complexes, biological studies 15766-00-4D, Samarium 153, conjugated complexes, biological studies 19253-88-4D, Trimethyl lysine, radiolabeled conjugates 20537-88-6D, Amifostine, radiolabeled conjugates 23214-92-8D, Doxorubicin, radiolabeled conjugates 24991-23-9D, radiolabeled conjugates 25513-46-6D, Polyglutamic acid, radiolabeled conjugates 25608-40-6D, Polyaspartic acid, radiolabeled conjugates 26063-13-8D, Polyaspartic acid, radiolabeled conjugates 39809-25-1D, Penciclovir, radiolabeled conjugates 55612-21-0D, FIRU, radiolabeled conjugates 69123-98-4D, Fiau, radiolabeled conjugates 82410-32-0D, Ganciclovir, radiolabeled conjugates 99685-96-8D, Fullerene, radiolabeled conjugates 104495-35-4D, radiolabeled conjugates 121563-65-3D, IVFRU, radiolabeled conjugates 154361-50-9, Capecitabine 154361-50-9D, Capecitabine, radiolabeled conjugates 162011-90-7D, Rofecoxib, radiolabeled conjugates 169590-42-5D, Celecoxib, radiolabeled conjugates 180288-69-1D, Herceptin, radiolabeled conjugates 202409-33-4D, Etoricoxib, radiolabeled conjugates 206067-83-6D, radiolabeled conjugates 211918-90-0D, radiolabeled conjugates 290374-12-8D, radiolabeled conjugates 290374-14-0D, radiolabeled conjugates 378784-45-3D, Technetium 99m, conjugated complexes, biological studies 693260-27-4 693260-27-4D, Tc-99 complexes 853731-91-6 853731-92-7
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(targeted radiolabeled ligands for tumor

imaging and therapy)
IT 3416-24-8D, reaction with ethylenedicysteine, Re-188 complexes 14378-26-8D, Re-188, complexes, biological studies 154069-62-2
RL: DGN (Diagnostic use); PKT (Pharmacokinetics); BIOL (Biological study); USES (Uses)
(targeted radiolabeled ligands for tumor imaging and therapy)
IT 443-48-1DP, Metronidazole, reaction product with ethylenedicysteineglucose, Re-188 complexes 86090-08-6DP, Angiostatin, radiolabeled conjugates 99685-96-8DP, [5,6]Fullerene-C60-Ih, reaction products with ethylenedicysteine, Tc-99 complexes 154069-62-2DP, conjugates 187888-07-9DP, Endostatin, radiolabeled conjugates 693260-07-0DP, Tc-99 complexes 693260-24-1DP, Tc-99 complexes 693260-30-9P 853731-93-8DP, Tc-99 complexes
RL: DGN (Diagnostic use); PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(targeted radiolabeled ligands for tumor imaging and therapy)
IT 119951-66-5P 693260-24-1P
RL: DGN (Diagnostic use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(targeted radiolabeled ligands for tumor imaging and therapy)
IT 58-60-6 85-87-0, Pyridoxamine 107-15-3, Ethylenediamine, reactions 2949-22-6, Ethyl isocyanatoacetate 14344-48-0, L,L-Ethylenedicysteine 14470-28-1 23284-33-5 39809-25-1, Penciclovir 99685-96-8, Fullerene 169590-42-5, Celecoxib
RL: RCT (Reactant); RACT (Reactant or reagent)
(targeted radiolabeled ligands for tumor imaging and therapy)
IT 206067-84-7P 693260-03-6P 693260-05-8P 693260-07-0P 693260-23-0P 853731-93-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(targeted radiolabeled ligands for tumor imaging and therapy)
IT 77-92-9, Citric acid, uses 87-69-4, Tartaric acid, uses 526-95-4, D-Gluconic acid 23351-51-1, Glucoheptonic acid 25525-21-7, Glucaric acid
RL: NUU (Other use, unclassified); USES (Uses)
(transchelator; targeted radiolabeled ligands for tumor imaging and therapy)

L60 ANSWER 7 OF 18 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:211145 HCAPLUS Full-text
DOCUMENT NUMBER: 143:73888
TITLE: Tumor specific imaging using Tc-99m and Ga-68 labeled radiopharmaceuticals
AUTHOR(S): Yang, David J.; Azhdarinia, Ali; Kim, E. Edmund
CORPORATE SOURCE: Department of Nuclear Medicine, The University of Texas M.D. Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE: Current Medical Imaging Reviews (2005), 1(1), 25-34
CODEN: CMIRCV; ISSN: 1573-4056
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ED Entered STN: 10 Mar 2005
AB A review. Improvement of scintigraphic tumor imaging is extensively determined by the development of more tumor specific radiopharmaceuticals. Thus, to improve the differential diagnosis, prognosis, planning and monitoring of cancer treatment, several

functional pharmaceuticals have been developed. Application of mol. targets for cancer imaging, therapy and prevention using generator-produced isotopes are the major focus of ongoing research projects. Radionuclide imaging modalities (positron emission tomog., PET; single photon emission computed tomog., SPECT) are diagnostic cross-sectional imaging techniques that map the location and concentration of radionuclide-labeled radiotracers. 99mTc- and 68Ga-labeled agents using ethylenedicysteine (EC) as a chelator were synthesized and their potential uses to assess tumor targets were evaluated. 99mTc (t1/2=6 h, 140 keV) is used for SPECT and 68Ga (t1/2=68 min, 511 keV) is for PET. Mol. targets labeled with Tc-99m and Ga-68 can be utilized for prediction of therapeutic response, monitoring tumor response to treatment and differential diagnosis. Mol. targets for oncol. research in (1) cell apoptosis, (2) gene and nucleic acid-based approach, (3) angiogenesis (4) tumor hypoxia, and (5) metabolic imaging are discussed. Numerous imaging ligands in these categories have been developed and evaluated in animals and humans. Mol. targets were imaged and their potential to redirect optimal cancer diagnosis and therapeutics were demonstrated.

CC 8-0 (Radiation Biochemistry)

ST review technetium 99 gallium 68 PET SPECT tumor diagnosis

IT Diagnosis
(cancer; tumor specific imaging using Tc-99m and Ga-68 labeled radiopharmaceuticals)

IT Diagnosis
(radiodiagnostic agents; tumor specific imaging using Tc-99m and Ga-68 labeled radiopharmaceuticals)

IT Angiogenesis
Apoptosis
Hypoxia
Positron-emission tomography
Single-photon-emission computed tomography
(tumor specific imaging using Tc-99m and Ga-68 labeled radiopharmaceuticals)

IT Imaging
(tumor; tumor specific imaging using Tc-99m and Ga-68 labeled radiopharmaceuticals)

IT 14133-76-7D, Technetium 99, ethylenedicysteine conjugates, biological studies 15757-14-9D, Gallium 68, ethylenedicysteine conjugates, biological studies
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(tumor specific imaging using Tc-99m and Ga-68 labeled radiopharmaceuticals)

REFERENCE COUNT: 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L60 ANSWER 8 OF 18 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:320164 HCAPLUS Full-text

DOCUMENT NUMBER: 142:88867

TITLE: Infection detection in mice using 99mTc-labeled HYNIC and N2S2 chelate conjugated to the antimicrobial peptide UBI 29-41

AUTHOR(S): Welling, Mick M.; Visentin, Roberta; Feitsma, Hans I. J.; Lupetti, Antonella; Pauwels, Ernest K. J.; Nibbering, Peter H.

CORPORATE SOURCE: Department of Radiology, Division of Nuclear Medicine, Leiden University Medical Center (LUMC), Leiden, 2300, Neth.

SOURCE: Nuclear Medicine and Biology (2004), 31(4), 503-509
CODEN: NMBIEO; ISSN: 0969-8051

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 20 Apr 2004

AB Earlier we reported that UBI 29-41, a synthetic peptide corresponding to residues 29-41 of human ubiquicidin, directly labeled with technetium-99m (99mTc-UBI 29-41) distinguishes bacterial and fungal infections from sterile inflammations in animals.

This study was undertaken to evaluate the radiochem. and biol. characteristics of 99mTc-UBI 29-41 labeled through the intermediacy of a HYNIC or N2S2 moiety, which were introduced at the N-terminus of UBI 29-41 during solid phase synthesis, with 99mTc-UBI 29-41. Methods were as follows: UBI 29-41 and HYNIC- or N2S2-conjugated peptide were labeled with technetium-99m. Prepns. of these radiolabeled UBI 29-41 were purified by HPLC and Sep-Pak. Next, the stability of these tracers in human serum was challenged for 24 h and their in vitro binding to bacteria assessed. Using scintigraphy up to 2 h after injection of the tracer and ex vivo counts at the last interval we evaluated the ability of the three tracers to detect bacterial infections in mice inoculated with 2+107 viable Staphylococcus aureus or Klebsiella pneumoniae as well as their biodistribution. We observed the following results: HPLC anal. of purified 99mTc-HYNIC-UBI 29-41, 99mTc-UBI 29-41 and 99mTc-N2S2-UBI 29-41 revealed that within 60 min >90% of the radioactivity was associated with the peptide. In addition, the stability of these radiolabeled UBI 29-41 peptides in human serum was excellent. All three tracers bound equally well to bacteria in vitro. After i.v. injection into mice with an exptl. bacterial infection 99mTc-HYNIC-UBI 29-41 and 99mTc-UBI 29-41 were rapidly removed from the circulation mainly by renal clearance (at t = 120 min approx. 60% of the injected dose/g tissue; % ID/g). In contrast, 99mTc-N2S2-UBI 29-41 was removed mainly by the liver (t = 120 min; 52% ID/g) showing deposits in the intestines (t = 120 min; 31% ID/g) and to a lesser extent by renal clearance (19% ID/g). All three tracers rapidly detected bacterial infections in mice and highest accumulation (target -to-nontarget ratios between 3.2 and 3.6 and between 2.9 and 4.4 for infections with S. aureus and K. pneumoniae, resp.) was found at 2 h after injection of the tracer. In conclusion, purified 99mTc-HYNIC-UBI 29-41 and 99mTc-N2S2-UBI 29-41 were as effective as 99mTc-UBI 29-41 in detecting infections in mice injected i.m. with bacteria. However, 99mTc-N2S2-UBI 29-41 should not be advised for the imaging of abdominal infections as this tracer, in contrast to the other tracers, is cleared via the liver and intestines.

CC 8-9 (Radiation Biochemistry)

ST infection technetium 99 HYNIC N2S2 conjugate antimicrobial peptide

IT Infection
(bacterial; infection detection in mice using 99mTc-labeled HYNIC and N2S2 chelate conjugated to antimicrobial peptide UBI 29-41)

IT Human
Klebsiella pneumoniae
Scintigraphic agents
Scintigraphy
Staphylococcus aureus
(infection detection in mice using 99mTc-labeled HYNIC and N2S2 chelate conjugated to antimicrobial peptide UBI 29-41)

IT 14133-76-7D, Technetium-99, complexes with UBI 29-41, biological studies 216867-99-1D, technetium-99 labeled, derivs.
RL: DGN (Diagnostic use); PKT (Pharmacokinetics); BIOL (Biological study); USES (Uses)
(infection detection in mice using 99mTc-labeled HYNIC and N2S2 chelate conjugated to antimicrobial peptide UBI 29-41)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L60 ANSWER 9 OF 18 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:54939 HCAPLUS Full-text

DOCUMENT NUMBER: 139:159553

TITLE: Assessment of epidermal growth factor receptor with 99mTc-ethylenedicysteine-C225 monoclonal antibody

AUTHOR(S): Schechter, Naomi R.; Yang, David J.; Azhdarinia, Ali; Kohanim, Sahar; Wendt, Richard, III; Oh, Chang-Sok; Hu, Mickey; Yu, Dong-Fang; Bryant, Jerry; Ang, K. Kian; Forster, Kenneth M.; Kim, E. Edmund; Podoloff, Donald A.

CORPORATE SOURCE: Div. Radiation Oncology, Univ. Texas, Houston, TX, USA

SOURCE: Anti-Cancer Drugs (2002), Volume Date 2003, 14(1), 49-56
CODEN: ANTDEV; ISSN: 0959-4973
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 23 Jan 2003

AB Epidermal growth factor receptor (EGFR) plays an important role in cell division and cancer progression, as well as angiogenesis and metastasis. Since many tumor cells exhibit the EGFR on their surface, functional imaging of EGFR provides not only a non-invasive, reproducible, quantifiable alternative to biopsies, but it also greatly complements pharmacokinetic studies by correlating clin. responses with biol. effects. Moreover, mol. endpoints of anti-EGFR therapy could be assessed effectively. C225 is a chimeric monoclonal antibody that targets the human extracellular EGFR and inhibits the growth of EGFR-expressing tumor cells. Also, it has been demonstrated that C225, in combination with chemotherapeutic drugs or radiotherapy, is effective in eradicating well-established tumors in nude mice. We have developed 99mTc-labeled C225 using ethylenedicysteine (EC) as a chelator. This study aimed at measuring uptake of 99mTc-EC-C225 in EGFR tumor-bearing animal models and preliminary feasibility of imaging patients with head and neck carcinomas. Western blot anal. and cytotoxicity assays were used to examine the integrity of EC-C225. Tissue distribution studies of 99mTc-EC-C225 were evaluated in tumor-bearing rodents at 0.5-4 h. biodistribution of 99mTc-EC-C225 in tumor-bearing rodents showed increased tumor-to-tissue ratios as a function of time. and biodistribution studies demonstrated the possibility of using 99mTc-EC-C225 to assess EGFR expression. SPECT images confirmed that the tumors could be visualized with 99mTc-EC-C225 from 0.5 to 4 h in tumor bearing rodents. We conclude that 99mTc-EC-C225 may be useful to assess tumor EGFR expression. This may be useful in the future for selecting patients for treatment with C225.

CC 1-6 (Pharmacology)
Section cross-reference(s): 8

ST technetium99m ethylenedicysteine C225 prepn pharmacokinetics EGFR imaging angiogenesisinhibitor human; epidermal growth factor receptor monoclonal antibody antiangiogenesis headneck carcinoma

IT Angiogenesis inhibitors
Antitumor agents
Blood
Brain
Drug bioavailability
Heart
Human
Intestine
Kidney
Liver
Lung
Mammary gland, neoplasm
Muscle
Scintigraphy
Single-photon-emission computed tomography
Spleen
Stomach
Thyroid gland
(assessment of epidermal growth factor receptor with 99mTc-ethylenedicysteine-C225 monoclonal antibody)

IT Epidermal growth factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(assessment of epidermal growth factor receptor with 99mTc-ethylenedicysteine-C225 monoclonal antibody)

IT Antibodies and Immunoglobulins
RL: DGN (Diagnostic use); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fusion products; assessment of epidermal growth factor receptor with 99mTc-ethylenedicysteine-C225 monoclonal antibody)

IT Carcinoma
Carcinoma
(head and neck squamous cell carcinoma; assessment of epidermal growth factor receptor with 99mTc-ethylenedicysteine

-C225 monoclonal antibody)
IT Antibodies and Immunoglobulins
RL: DGN (Diagnostic use); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal, labeled; assessment of epidermal growth factor receptor with 99mTc-ethylenedicysteine-C225 monoclonal antibody)
IT Head and neck, neoplasm
Head and Neck, neoplasm
(squamous cell carcinoma; assessment of epidermal growth factor receptor with 99mTc-ethylenedicysteine-C225 monoclonal antibody)
IT Radiography
(tumor; assessment of epidermal growth factor receptor with 99mTc-ethylenedicysteine-C225 monoclonal antibody)
IT 14133-76-7DP, Technetium-99, IMC-C225-ethylenedicysteine complex, biological studies
14344-48-0DP, L,L-Ethylenedicysteine, 99mTc-IMC-C225 complex chelated with 205923-56-4DP, IMC-C225, technetium-99-ethylenedicysteine complex
RL: DGN (Diagnostic use); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(assessment of epidermal growth factor receptor with 99mTc-ethylenedicysteine-C225 monoclonal antibody)
IT 34592-47-7, L-Thiazolidine-4-carboxylic acid
RL: PRP (Properties); RCT (Reactant); RACT (Reactant or reagent)
(assessment of epidermal growth factor receptor with 99mTc-ethylenedicysteine-C225 monoclonal antibody)
IT 23288-61-1, Pertechnetate labeled with technetium 99
25952-53-8, 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride 82436-78-0, Sulfo-N-hydroxysuccinimide
RL: RCT (Reactant); RACT (Reactant or reagent)
(assessment of epidermal growth factor receptor with 99mTc-ethylenedicysteine-C225 monoclonal antibody)
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L60 ANSWER 10 OF 18 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:849373 HCAPLUS Full-text
DOCUMENT NUMBER: 137:358081
TITLE: Diagnostic imaging compositions, their methods of synthesis, and use
INVENTOR(S): Li, Chun; Wen, Xiaoxia; Wu, Qing-Ping; Wallace, Sydney; Ellis, Lee M.
PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002087498	A2	20021107	WO 2002-US12510	20020419
WO 2002087498	A3	20031030		
WO 2002087498	A8	20031211		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,

NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,
TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI,
FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG,
CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2444483	A1	20021107	CA 2002-2444483	20020419
US 2002197261	A1	20021226	US 2002-126369	20020419
US 2003003048	A1	20030102	US 2002-126216	20020419
EP 1389090	A2	20040218	EP 2002-766783	20020419

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,
PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.:	US 2001-286453P	P 20010426
	US 2001-334969P	P 20011204
	US 2001-343147P	P 20011220
	WO 2002-US12510	W 20020419

ED Entered STN: 08 Nov 2002

AB Conjugate mols. comprising a ligand bonded to a polymer are disclosed. One such conjugate mol. comprises a ligand bonded to a polymer, a chelating agent bonded to the polymer, and a radioisotope chelated to the chelating agent. The conjugate mols. may be useful in detecting and/or treating tumors or biol. receptors. These conjugate mols. may be synthesized without the necessity of preactivation of the ligand using an SCN-polymer-chelating agent precursor. Conjugate mols. incorporating an annexin V ligand are particularly useful for visualizing apoptotic cells. Conjugate mols. incorporating a C225 ligand are particularly useful for targeting tumors expressing EGFR.

IC ICM A61K

CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1, 8

ST indium lll antibody annexin conjugate tumor ~~imaging~~;
immunoconjugate radiolabeled tumor ~~targeting~~

IT Bone, neoplasm
Brain, neoplasm
Diagnostic agents
Drug delivery systems
Drug toxicity
Head and Neck, neoplasm
Head and Neck, neoplasm
Human
Hypoxia
Infection
Inflammation
Leukemia
Liver, neoplasm
Lung, neoplasm
Mammary gland, neoplasm
Multiple sclerosis

Neoplasm
Ovary, neoplasm
Pancreas, neoplasm
Positron-emission tomography
Prostate gland, neoplasm
Radiopharmaceuticals
Regeneration, animal
Rheumatoid arthritis
Scintigraphy
Sickle cell anemia
Single-photon-emission computed tomography
Surgery
Thalassemia
Transplant rejection
(diagnostic imaging compns. comprising radiolabeled conjugates)

IT 60-00-4D, EDTA, radiolabeled conjugates 295-37-4D, Cyclam, radiolabeled conjugates 365-08-2D, DTTP, radiolabeled conjugates 482-54-2D, 1,2-Cyclohexanediamine-N,N,N',N'-tetraacetic acid, radiolabeled conjugates 1429-50-1D, EDTMP, radiolabeled conjugates 2418-14-6D, Dimercaptosuccinic acid, radiolabeled conjugates 2809-21-4D, HEDP, radiolabeled conjugates 3565-84-2D, Cy-DTPA, radiolabeled conjugates 3599-32-4, Indocyanine green 9002-89-5D, Polyvinyl alcohol, radiolabeled conjugates 9003-01-4D, Polyacrylic acid, radiolabeled conjugates 9003-39-8D, Polyvinyl pyrrolidone, radiolabeled conjugates 9004-54-0D, Dextran, radiolabeled conjugates 9004-61-9D, Hyaluronic acid, radiolabeled conjugates 9012-76-4D, Chitosan, radiolabeled conjugates 9044-05-7D, Carboxymethyl dextran, radiolabeled conjugates 10098-91-6D, Yttrium 90, radiolabeled conjugates, biological studies 13981-25-4D, Copper 64, radiolabeled conjugates, biological studies 14119-09-6D, Gallium 67, conjugates labeled with, biological studies 14344-48-0D, radiolabeled conjugates 14391-63-0D, Rubidium 82, conjugates labeled with, biological studies 14809-53-1D, Yttrium 86, radiolabeled conjugates, biological studies 15064-65-0D, Thallium 201, radiolabeled conjugates, biological studies 15735-70-3D, Platinum 193, radiolabeled conjugates, biological studies 15757-14-9D, Gallium 68, conjugates labeled with, biological studies 15757-86-5D, Copper 67, radiolabeled conjugates, biological studies 15827-60-8D, DTPMP, radiolabeled conjugates 25104-13-6D, Poly(D-glutamic acid), radiolabeled conjugates 25104-18-1D, Polylysine, radiolabeled conjugates 25322-69-4D, Polypropylene oxide, radiolabeled conjugates 25608-40-6D, Poly(L-aspartic acid), radiolabeled conjugates 26063-13-8D, Poly(L-aspartic acid), radiolabeled conjugates 27878-59-7D, Poly(2-hydroxyethyl L-glutamine), radiolabeled conjugates 27881-01-2D, Poly(D-aspartic acid), radiolabeled conjugates 27881-03-4D, Poly(DL-aspartic acid), radiolabeled conjugates 38000-06-5D, Polylysine, radiolabeled conjugates 49717-32-0D, radiolabeled conjugates 60239-18-1D, DOTA, radiolabeled conjugates 60239-20-5D, TRITA, radiolabeled conjugates 60239-22-7D, TETA, radiolabeled conjugates 62031-54-3D, FGF, radiolabeled conjugates 62229-50-9D, EGF, radiolabeled conjugates 72772-21-5D, radiolabeled conjugates 86090-08-6D, Angiostatin, radiolabeled conjugates 91987-74-5D, DOTP, radiolabeled conjugates 104162-48-3D, DOTMA, radiolabeled conjugates 113786-33-7D, BOPTA, radiolabeled conjugates 120041-08-9D, HP-DO3A, radiolabeled conjugates 120041-09-0D, radiolabeled conjugates 131418-52-5D, radiolabeled conjugates 132446-35-6D, DOTMP, radiolabeled conjugates 133081-24-0D, 6-Hydrazinonicotinic acid, radiolabeled conjugates 136705-18-5D, DOTEP, radiolabeled conjugates 138149-64-1D, DOTPP, radiolabeled conjugates 145089-54-9D, DOTBzP, radiolabeled conjugates 158414-87-0D, Cy2-DTPA, radiolabeled conjugates 161167-43-7D, DOTPME, radiolabeled conjugates 174722-31-7D, Rituxan, radiolabeled conjugates 180288-69-1D, Herceptin, radiolabeled conjugates 186270-49-5D, Angiopoietin 1, radiolabeled conjugates 187888-07-9D, Endostatin, radiolabeled conjugates 194368-66-6D,

Angiopoietin 2, radiolabeled conjugates 215369-21-4D, DC101, radiolabeled conjugates 221230-66-6D, radiolabeled conjugates 244082-19-7D, radiolabeled conjugates 474424-15-2D, radiolabeled conjugates
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(diagnostic imaging compns. comprising radiolabeled conjugates)
IT 14133-76-7D, Technetium 99, radiolabeled conjugates, biological studies 14885-78-0D, Indium 113, radiolabeled conjugates, biological studies
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(metastable; diagnostic imaging compns. comprising radiolabeled conjugates)

L60 ANSWER 11 OF 18 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:449640 HCAPLUS Full-text
DOCUMENT NUMBER: 137:33538
TITLE: Preparation of amino acid derivatives used as perturbed membrane-binding compounds for diagnostic and therapeutic applications
INVENTOR(S): Ziv, Ilan; Shirvan, Anat; Ebner, Sharon
PATENT ASSIGNEE(S): NST Neurosurvival Technologies Ltd., Israel
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002046147	A2	20020613	WO 2001-IB2282	20011203
WO 2002046147	A3	20031224		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2436601	A1	20020613	CA 2001-2436601	20011203
AU 2002018431	A5	20020618	AU 2002-18431	20011203
EP 1401420	A2	20040331	EP 2001-999555	20011203
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
BR 2001015970	A	20040810	BR 2001-15970	20011203
JP 2004528275	T	20040916	JP 2002-547886	20011203
US 2004082499	A1	20040429	US 2003-433668	20030310
US 2005244812	A1	20051103	US 2005-172934	200507

PRIORITY APPLN. INFO.: IL 2000-140114 A 05
200012
06

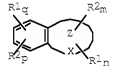
IL 2001-141571 A
200102
21

IL 2001-145210 A
200108
30

WO 2001-IB2282 W
200112
03

US 2003-433668 A2
200310
31

OTHER SOURCE(S): MARPAT 137:33538
ED Entered STN: 14 Jun 2002
GI



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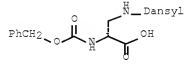
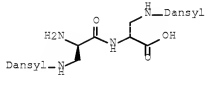


II



III

AB The present invention provides preparation and uses of perturbed membrane-binding compds. (PMBC) I that bind selectively to cells undergoing perturbations and alterations of their normal membrane organization, while binding to a lesser degree to cell having membranes of normal organization [Z =cycloalkyl, cycloalkenyl, heterocyclyl, aryl, heteroaryl; X = CH, CH2, N, NH, O, S; n, m, q, p = 0-1; wherein n + q = 1; m + p = 1; R1 = A, L-A; L = D, U, U-D, D-U, D-U-O, O-U-D, D-U-NH, NH-U-D, D-U-D, U-D-U; U = H, alkylene, alkenylene, cycloalkenylene, aryl, heterocycloalkylene, heterocycloalkenylene, heteroaryl; D = O, SO0-2, SO2NH, NHSO2, NH, PO, PO2, PO2H, etc,; A = charged moieties at pH of about 7 when e = 1; when e = 2 or 3, A = polar uncharged moieties and charged moieties at pH of about 7; R2 = WR3b; W = null, secondary or tertiary amine, O, S, D; R3 = H, alkyl, alkenyl, b = 1-3; when e = 2 or 3, the C groups are linked to each other either directly or through an L moiety]. I can selectively bind to cells undergoing perturbation of their normal organization of membrane (PNOM), while binding to a much lesser degree to cells which maintain the normal organization of their membrane. The selective binding of I may be used for detection of cells or cell-derived particles, which contain perturbed membranes (PM) used for the diagnosis of diseases in which cells undergo PNOM or in a therapeutic application used to target therapeutically useful drugs to organs and tissues in the body wherein PNOM occurs, e.g., regions of cell death, thrombus formation or inflammation and also to clear body fluids from cells having PM, or of larger structures comprising such membranes, such as

emboli circulating in the blood. Examples include synthesis of several examples of I, binding of I to activated red blood cells, apoptotic cells, activated platelets, detection of apoptotic cells in-vivo within a tumor and detection of chemotherapy-induced apoptosis of small intestine epithelium. For instance, D-Z-asparagine was converted in 4 steps to II. The deprotected Me ester of II was coupled to II (DCC, NHS) and the adduct saponified and deprotected to give III.

IC ICM C07C0311-00
CC 34-3 (Amino Acids, Peptides, and Proteins)
IT Fluorescence
Positron-emission tomography
Tomography
X-ray
(method for detection of peptide derivs. used to identify cells undergoing perturbation of normal organization of membrane)
IT X-ray spectroscopy
(radioisotope-induced, Tc-99, In-111; method for detection of peptide derivs. used to identify cells undergoing perturbation of normal organization of membrane)
IT 84295-19-2 202582-38-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(linker for drugs to solid phase; metal chelators; amino acid derivs. as perturbed membrane-binding compds. for diagnostic and therapeutic applications)

L60 ANSWER 12 OF 18 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:446909 HCAPLUS Full-text
DOCUMENT NUMBER: 138:1753
TITLE: Assessment of antiangiogenic effect using 99mTc-EC-endostatin
AUTHOR(S): Yang, David J.; Kim, Kil-Dong; Schechter, Naomi R.; Yu, Dong-Fang; Wu, Peng; Azhdarinia, Ali; Roach, Jennifer S.; Kalimi, Saady K.; Ozaki, Kaoru; Fogler, William E.; Bryant, Jerry L.; Herbst, Roy; Abbruzzes, James; Kim, E. Edmund; Podoloff, Donald A.
CORPORATE SOURCE: Department of Nuclear Medicine, The University of Texas M. D. Anderson Cancer Center, Houston, TX, USA
SOURCE: Cancer Biotherapy & Radiopharmaceuticals (2002), 17(2), 233-246
CODEN: CBRAFJ; ISSN: 1084-9785
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 14 Jun 2002
AB Tumor vascular d. may provide a prognostic indicator of metastatic potential or survival. The purpose of this study was to develop 99mTc-ethylenedicysteine-endostatin (99mTc-EC-endostatin) for the evaluation of anti-angiogenesis therapy. 99mTc-EC-endostatin was prepared by conjugating ethylenedicysteine (EC) to endostatin, followed by adding pertechnetate and tin chloride. Radiochem. purity was >95%. In vitro cell viability, affinity and TUNEL assays were performed. Tissue distribution and planar imaging of radiolabeled endostatin were determined in tumor-bearing rats. To assess anti-angiogenic treatment response, rats were treated with endostatin, paclitaxel and saline, followed by imaging with 99mTc-EC-endostatin. Tumor response to endostatin therapy in tumor-bearing animal models was assessed by correlating tumor uptake dose with microvessel d., VEGF, bFGF and IL-8 expression during endostatin therapy. Results: In vitro cell viability and TUNEL assays indicated no marked difference between EC-endostatin and endostatin. Cellular uptake assay suggests that endostatin binds to endostatin receptor. Biodistribution of 99mTc-EC-endostatin in tumor-bearing rats showed increased tumor-to-tissue count d. ratios as a function of time. Tumor uptake (%ID/g) of 99mTc-EC-endostatin was 0.2-0.5. Planar images confirmed that the tumors could be visualized clearly with 99mTc-EC-endostatin. The optimal time for imaging using radiolabeled endostatin was 2 h. 99mTc-EC-endostatin could assess treatment response. There was a correlation between tumor uptake and cellular targets expression. The results indicate that it is feasible to use 99mTc-EC-endostatin to assess efficiency of anti-angiogenesis therapy.
CC 8-9 (Radiation Biochemistry)

Section cross-reference(s): 1
ST technetium 99m ethylenedicysteine endostatin angiogenesis inhibitor tumor imaging
IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(endostatin, endostatin binding to; 99mTc-ethylenedicysteine-endostatin for evaluation of anti-angiogenesis therapy)
IT Imaging
(tumor; 99mTc-ethylenedicysteine-endostatin for evaluation of anti-angiogenesis therapy)
IT Angiogenesis inhibitors
(99mTc-ethylenedicysteine-endostatin for evaluation of anti-angiogenesis therapy)
IT 14133-76-7DP, 99Tc, endostatin-ethylenedicystein conjugate labeled with, biological studies 14344-48-0DP, L,L-Ethylenedicysteine, endostatin conjugate, 99Tc-labeled 187888-07-9DP, Endostatin, ethylenedicystein conjugate, 99Tc-labeled
RL: DGN (Diagnostic use); PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(99mTc-ethylenedicysteine-endostatin for evaluation of anti-angiogenesis therapy)
IT 33069-62-4, Paclitaxel
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(99mTc-ethylenedicysteine-endostatin for evaluation of anti-angiogenesis therapy)
IT 1892-57-5, 1-Ethyl-3-(3-dimethylaminopropyl) carbo-diimide 82436-78-0, N-Hydroxysulfosuccinimide
RL: RCT (Reactant); RACT (Reactant or reagent)
(99mTc-ethylenedicysteine-endostatin for evaluation of anti-angiogenesis therapy)
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L60 ANSWER 13 OF 18 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:796001 HCAPLUS Full-text
TITLE: Chlorophyll-a based bis-aminoethanethiol and modified DTPA conjugates as diagnostic and therapeutic agents.
AUTHOR(S): Li, Guolin; Ma, Bing; Grossman, Zachary; Dougherty, Thomas J.; Pandey, Ravindra K.
CORPORATE SOURCE: Nuclear Medicine, Roswell Park Cancer Institute, Buffalo, NY, 14263, USA
SOURCE: Abstracts of Papers, 220th ACS National Meeting, Washington, DC, United States, August 20-24, 2000 (2000) MEDI-004
CODEN: 69FZC3
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; Meeting Abstract
LANGUAGE: English
ED Entered STN: 14 Nov 2000
AB In order to develop long-wavelength absorbing photosensitizers for photodynamic therapy (PDT), certain chlorophyll a analogs demonstrated high tumor uptake and proved to be efficient photosensitizers for the treatment of various types of cancers. Recently, we have developed efficient methodologies for the preparation of the corresponding N2S2 and modified DTPA conjugates. These chelates are "bifuctional" because, they are capable to bind to Tc-99m (N2S2 ligand), In-111 and Gd (modified DTPA ligand) at one site and target specific vehicles (photosensitizers) at the other end. Interestingly, the presence of the ligating groups did not diminish their singlet oxygen producing efficacy, a key cytotoxic agent for the destruction of tumors by PDT. The high uptake of these conjugates, therefore, presents the possibility of using a single mol. for both successful nuclear imaging and then for photodynamic therapy. The synthesis and preliminary biol. data obtained from these compds. will be presented.

L60 ANSWER 14 OF 18 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:797954 HCAPLUS Full-text
DOCUMENT NUMBER: 132:160324
TITLE: Synthesis of N2S2 conjugates of the highly specific mitochondrial diazepam binding inhibitor (DBI) receptor complexes
AUTHOR(S): Li, Guolin; Ma, Bing; Missert, Joseph R.; Grossman, Zachary D.; Pandey, Ravindra K.
CORPORATE SOURCE: Department of Nuclear Medicine, Roswell Park Cancer Institute, Buffalo, NY, 14263, USA
SOURCE: Heterocycles (1999), 51(12), 2855-2860
CODEN: HTCYAM; ISSN: 0385-5414
PUBLISHER: Japan Institute of Heterocyclic Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 19 Dec 1999
AB A novel approach for the synthesis of N2S2 ligands conjugated with 2-phenylindole analogs known as mitochondrial diazepam binding inhibitor receptor complexes (previously known as peripheral-type benzodiazepine receptor), as possible target specific 99mTc imaging agents is described.
CC 78-7 (Inorganic Chemicals and Reactions)
Section cross-reference(s): 1, 8, 27
ST mitochondrial DBI receptor phenylindole conjugate prepn; technetium phenylindole conjugate mitochondrial DBI receptor prepn
IT Proteins, specific or class
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(DBI (diazepam binding inhibitor); preparation of phenylindole analogs of N2S2 conjugates of highly specific mitochondrial diazepam binding inhibitor (DBI) receptor complexes as possible target specific 99mTc imaging agents)
IT Benzodiazepine receptors
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(peripheral-type; preparation of phenylindole analogs of N2S2 conjugates of highly specific mitochondrial diazepam binding inhibitor (DBI) receptor complexes as possible target specific 99mTc imaging agents)
IT Imaging agents
(preparation of phenylindole analogs of N2S2 conjugates of highly specific mitochondrial diazepam binding inhibitor (DBI) receptor complexes as possible target specific 99mTc imaging agents)
IT 96-32-2, Methyl bromoacetate 124-09-4, 1,6-Hexanediamine, reactions 156-57-0, 2-Aminoethanethiol hydrochloride 824-94-2, p-Methoxybenzyl chloride 4567-06-0 23288-61-1, 99-Tc -pertechnetate 152863-83-7 257881-23-5 257881-24-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(for preparation of phenylindole analogs of N2S2 conjugates of highly specific mitochondrial diazepam binding inhibitor (DBI) receptor complexes as possible target specific 99mTc imaging agents)
IT 4662-03-7P 22876-65-9P 193481-73-1P 228253-42-7P 257881-21-3P 257881-22-4P 257881-27-9P 257881-28-0P 257881-29-1P 257881-30-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(for preparation of phenylindole analogs of N2S2 conjugates of highly specific mitochondrial diazepam binding inhibitor (DBI) receptor complexes as possible target specific 99mTc imaging agents)
IT 257881-25-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(for preparation of phenylindole analogs of N2S2 conjugates of highly specific mitochondrial diazepam binding inhibitor (DBI) receptor

complexes as possible target specific 99mTc imaging agents)

IT 257881-31-5P 257881-32-6P 257881-33-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of phenylindole analogs of N2S2 conjugates of highly specific mitochondrial diazepam binding inhibitor (DBI) receptor complexes as possible target specific 99mTc imaging agents)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L60 ANSWER 15 OF 18 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:347814 HCAPLUS Full-text
DOCUMENT NUMBER: 127:30947
TITLE: Clinical evaluation of technetium -99m-L,L-ethylenedicysteine in patients with chronic renal failure
AUTHOR(S): Prvulovich, Elizabeth M.; Bomanji, Jamshed B.; Waddington, Wendy A.; Rudrasingham, Ponnuthurai; Verbruggen, Alfons M.; Ell, Peter J.
CORPORATE SOURCE: Inst. Nuclear Medicine, Univ. College London Medical School, London, UK
SOURCE: Journal of Nuclear Medicine (1997), 38(5), 809-814
CODEN: JNMEAQ; ISSN: 0161-5505
PUBLISHER: Society of Nuclear Medicine
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 04 Jun 1997
AB Technetium-99m-L,L-ethylenedicysteine (99mTc-L,L-EC), a new renal radiopharmaceutical, has been shown to have similar excretion characteristics but a higher plasma clearance than 99mTc-mercaptoacetyltriglycine (99mTcMAG3) in normal volunteers and patients with obstructive nephropathy. This study evaluated 99mTc-L,L-EC in patients with chronic renal failure. The clearance of 99mTc-L,L-EC was compared with that of 125I-hippuran in 26 patients with varying degrees of chronic renal impairment (serum creatinine 168-1163 μmol/L). All 26 patients also were imaged with 99mTc-L,L-EC (70-80 MBq). Fifteen patients had further imaging with 99mTc-MAG3 (100 MBq) the following day. A subjective anal. of the 99mTc-L,L-EC images revealed that all were of acceptable quality regardless of creatinine level. In the 15 patients who were imaged with both 99mTc-L,L-EC and 99mTc-MAG3, general image quality and target-to-background ratios were similar. Time-activity curves and mean parenchymal transit times obtained with the two agents were almost identical. Plasma clearance values (mean ± s.d.) of 99mTc-L,L-EC and 125I-hippuran were 81±68 mL/min and 114±104 mL/min, resp. Mean 99mTc-L,L-EC clearance was 71% of the mean 125I-hippuran value. Technetium -99m-L,L-EC provides equally high-quality images to 99mTcMAG3 in patients with chronic renal failure. Technetium-99m-L,L-EC clearance more closely resembles that of hippuran than doses 99mTc-MAG3 clearance. These features together with its ease of preparation make 99mTc-L,L-EC an attractive alternative to 99mTc-MAG3 in patients with chronic renal failure.
CC 8-9 (Radiation Biochemistry)
ST technetium 99m ethylenedicysteine kidney failure imaging
IT Imaging
(clin. evaluation of technetium-99m-L,L-ethylenedicysteine in human patients with chronic renal failure)
IT Kidney, disease
(failure, chronic; clin. evaluation of technetium -99m-L,L-ethylenedicysteine in human patients with chronic renal failure)
IT 154069-62-2
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PROC (Process); USES (Uses)
(clin. evaluation of technetium-99m-L,L-

ethylenedicysteine in human patients with chronic renal failure)
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L60 ANSWER 16 OF 18 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:869518 HCAPLUS Full-text
DOCUMENT NUMBER: 123:250202
TITLE: Preparation of radiolabeled annexins for diagnostic imaging of thrombi
INVENTOR(S): Kasina, Sudhakar; Dewhurst, Timothy A.; Reno, John M.; Tait, Jonathan; Stratton, John
PATENT ASSIGNEE(S): Neorx Corp., USA
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9519791	A1	19950727	WO 1995-US953	19950123
W: CA, JP, US RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2180555	A1	19950727	CA 1995-2180555	19950123
CA 2180555	C	20041214		
EP 743861	A1	19961127	EP 1995-913955	19950123
EP 743861	B1	20030416		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, PT, SE				
JP 09509050	T	19970916	JP 1995-519734	19950123
JP 3664727	B2	20050629		
AT 237366	T	20030515	AT 1995-913955	19950123
WO 9534315	A1	19951221	WO 1995-US7599	19950613
W: CA, JP RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
JP 10504534	T	19980506	JP 1995-502468	19950613
EP 1364964	A1	20031126	EP 2003-11344	19950613
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT				
CA 2206274	A1	19960613	CA 1995-2206274	19951206
WO 9617618	A1	19960613	WO 1995-US15851	19951206
W: CA, JP RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT,				

	SE			
EP 799050	A1	19971008	EP 1995-942562	199512 06
EP 799050	B1	20040811		
R: DE, FR, GB				
JP 10512852	T	19981208	JP 1995-517741	199512 06
EP 1486509	A2	20041215	EP 2004-18920	199512 06
EP 1486509	A3	20050323		
R: DE, FR, GB				
PRIORITY APPLN. INFO.:			US 1994-185660 A2	199401 24
			US 1994-261064 A	199406 16
			US 1994-351653 A	199412 07
			WO 1995-US953 W	199501 23
			EP 1995-923885 A3	199506 13
			WO 1995-US7599 W	199506 13
			EP 1995-942562 A3	199512 06
			WO 1995-US15851 W	199512 06

ED Entered STN: 21 Oct 1995

AB Radiolabeled annexins useful for imaging vascular thrombi are diclosed, as are methods for their preparation A procedure is described for preparing an annexin V-N2S2 chelate conjugate containing 99mTc; the conjugate was used in thrombus imaging. Also described are a method for producing a cell expression clone of annexin V and a procedure for modifying annexin V.

IC ICM A61K0043-00
ICS A61K0037-00

CC 8-9 (Radiation Biochemistry)

IT Plasmid and Episome
(pET-12a-PAP1, 3/7/94, clone 1; radiolabeled annexin conjugate preparation for diagnostic imaging of thrombi)

IT Coordination compounds
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chelates, conjugates, N2S2; radiolabeled annexin conjugate preparation for diagnostic imaging of thrombi)

IT 14133-76-7, Technetium-99, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(metastable; radiolabeled annexin conjugate preparation for diagnostic imaging of thrombi)

L60 ANSWER 17 OF 18 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:204047 HCAPLUS Full-text
DOCUMENT NUMBER: 118:204047
TITLE: Dicarboxylate diamide dimercaptide (N2S2) technetium-99m complexes: synthesis and biological evaluation as potential renal radiopharmaceuticals
AUTHOR(S): Canney, Daniel J.; Billings, Jeffrey; Francesconi, Lynn C.; Guo, Yu Zhi; Haggerty, Brian S.; Rheingold, Arnold L.; Kung, Hank F.
CORPORATE SOURCE: Dep. Radiol., Univ. Pennsylvania, Philadelphia, PA, 19104, USA
SOURCE: Journal of Medicinal Chemistry (1993), 36(8), 1032-40
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 14 May 1993
AB Diamide dimercaptide (N2S2) ligands PhC(O)SCH(R)CONHCH2CH2NHCOCH2(R)CH2SC(O)Ph (4, 8, R = CH2COOMe, COOEt, resp.) and PhC(O)SCH(COOMe)CH2CONHCH2CH2NHCOCH2CH(COOMe)SC(O) Ph (5) were synthesized and evaluated as potential renal radiopharmaceuticals. The target compds. were prepared in modest overalls yields of 22%, 20%, and 19%, for 4, 8, and 5 resp., using readily available starting materials. Following in situ deprotection, 99mTc complexes of high radiochem. purity were obtained and are stable for ≤6 h. AsPh4[99TcO(L8)] [I, H4L8 = HSCH(COOEt)CONHCH2CH2NHCOCH(COOEt)SH] was isolated. X-ray crystallog. data for I (monoclinic, space group P21/n, Z = 4, R = 0.0645 and Rw = 0.0663) show that the Tc is bound to both thiolate S atoms and to 2 deprotonated amide N atoms. The coordination geometry about the Tc is square-pyramidal with an oxo ligand in the apical position. The Tc-N bond distances (2.002(12) and 1.984(12) Å), the Tc-S bond distances (2.300(5) and 2.286(5) Å), and the Tc-O bond distance (1.667(11) Å) are in good agreement with bond lengths reported for similar complexes. The carboxylate groups are not bonded to the Tc atom in the solid state, nor in CDCl3 solution, as evidenced by x-ray crystal data and solution NMR data, resp. In the solid state, I is monoanionic, therefore, at physiol. pH, [99mTcO(L8)] is presumably trianionic. Biodistribution studies performed in rats with the 99mTc complexes revealed slow blood clearance and high muscle uptake for these agents. Modest hepatobiliary excretion was observed, and low quantities of the complexes were found in the heart, lungs, and spleen after 1 h. The urinary excretion of the 99mTc complexes of ligands 4, 5, and 8 is slow when compared to the excretion of [131I]OIH in rats (22%, 22%, and 32% vs. 85-86%, resp.). Protein binding of 99mTc complexes of ligands 4, 5, and 8 in both rat and monkey plasma is similar to MAG3. Preliminary planar imaging studies in monkeys revealed slow renal excretion for these agents. The evaluated 99mTc complexes are poor candidates as renal radiopharmaceuticals.
CC 78-7 (Inorganic Chemicals and Reactions)
Section cross-reference(s): 8, 25, 75
ST crystal structure technetate oxo ethanediylmercaptoacetamidato complex; mercaptoacetamidato ethanediyl technetate oxo complex; renal excretion technetium ethanediylmercaptoacetamidato complex; biodistribution technetium ethanediylmercaptoacetamidato complex; protein plasma binding technetium ethanediylmercaptoacetamidato complex
IT Organ
(biodistribution of metastable technetium ethanediylmercaptoacetamidato complexes)
IT Proteins, biological studies
RL: BIOL (Biological study)
(technetium-99m ethanediylmercaptoacetamidato complexes binding of, of blood plasma)
IT Kidney, metabolism
(technetium-99m ethanediylmercaptoacetamidato complexes excretion by, in rats)

L60 ANSWER 18 OF 18 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1992:443632 HCAPLUS Full-text
DOCUMENT NUMBER: 117:43632
TITLE: Technetium- and rhenium-labeled

progestins: synthesis, receptor binding and in vivo distribution of an 11β-substituted progestin labeled with technetium-99 and rhenium-186

AUTHOR(S): DiZio, James P.; Anderson, Carolyn J.; Davison, Alan; Ehrhardt, Gary J.; Carlson, Kathryn E.; Welch, Michael J.; Katzenellenbogen, John A.

CORPORATE SOURCE: Dep. Chem., Univ. Illinois, Urbana, IL, 61801, USA

SOURCE: Journal of Nuclear Medicine (1992), 33(4), 558-69
CODEN: JNMEAQ; ISSN: 0161-5505

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 08 Aug 1992

AB In an effort to develop radiopharmaceuticals useful for the diagnostic imaging of steroid receptor-pos. breast tumors, an analog of the antiprogestin RU486 (mifepristone), modified to incorporate an N2S2 chelate system in the 11β-position, with 99Tc, 99mTc, and 186Re. For the 99Tc-labeled analogs, a syn pair and two individual antidiasteromers (linker methylene vs. metal-oxo, relative to the N2S2 plate) were isolated. In competitive radiometric binding assays, the syn pair had affinity for the progesterone receptor that was 25% that of (promegestone) R5020 (or 161% that of progesterone), and the individual antidiastereomers had affinities of 47% and 7% that of R5020 (or 303% and 45% that or progesterone). The specific-to-nonspecific binding ratio of the 99nTc and 186Re 11β-linked syn systems are 75/25 and 54/46, resp. In vivo, these conjugates showed progesterone receptor-mediated uptake in rat uterus, but also high uptake in non-target tissues, presumably because of the high lipophilicity of the metal complexes. Modified systems may be useful in vivo as receptor-directed agents for diagnostic imaging or treatment of steroid receptor-pos. tumors.

CC 8-9 (Radiation Biochemistry)
Section cross-reference(s): 32, 78

ST progesterone receptor binding technetium 99m prepn; receptor progesterone binding rhenium 186 complex

IT Imaging
(of mammary cancer, technetium- and rhenium-labeled progestins for)

IT Blood
Bone, metabolism
Brain, metabolism
Kidney, metabolism
Liver, metabolism
Lung, metabolism
Muscle, metabolism
Ovary, metabolism
Fats and Glyceridic oils
RL: BIOL (Biological study)
(technetium- and rhenium-labeled progestins distribution in)

IT Mammary gland
(neoplasm, imaging of, by technetium- and rhenium-labeled progestins)

IT Receptors
RL: BIOL (Biological study)
(progestogen, technetium- and rhenium-labeled progestins binding of, in vivo distribution in relation to)

IT Progestogens
RL: BIOL (Biological study)
(receptors, technetium- and rhenium-labeled progestins binding of, in vivo distribution in relation to)

IT 142287-16-9
RL: BIOL (Biological study)
(technetium-99m and rhenium-186 labeling of, receptor binding and in vivo distribution of)

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     FILE 'HCAPLUS' ENTERED AT 09:50:06 ON 12 JAN 2007
L11         7720 SEA ABB=ON  PLU=ON  YANG D?/AU
L12         4098 SEA ABB=ON  PLU=ON  YU D?/AU
L13         1582 SEA ABB=ON  PLU=ON  OH C?/AU
L14          681 SEA ABB=ON  PLU=ON  BRYANT J?/AU
L15            7 SEA ABB=ON  PLU=ON  L11 AND L12 AND L13 AND L14


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L15  ANSWER 1 OF 7  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2005:524970  HCAPLUS  Full-text
DOCUMENT NUMBER:          143:48042
TITLE:                    N2S2 chelate-targeting ligand conjugates
INVENTOR(S):              Yang, David J.; Yu, Dong-fang
                          ; Oh, Chang-Sok; Bryant, Jerry
                          L.
PATENT ASSIGNEE(S):       Board of Regents, the University of Texas
                          System, USA; Cell Point LLC
SOURCE:                   U.S. Pat. Appl. Publ., 68 pp.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ----------------    ----   --------    --------------------
     --------
     US 2005129619        A1    20050616    US 2003-732919
                                                                   200312
                                                                   10
PRIORITY APPLN. INFO.:                      US 2003-732919
                                                                   200312
                                                                   10

OTHER SOURCE(S):          MARPAT 143:48042
```

ED Entered STN: 17 Jun 2005
AB The invention provides, in a general sense, a new labeling strategy employing compds. that are N2S2 chelates conjugated to a targeting ligand, wherein the targeting ligand is a disease cell cycle targeting compound, a tumor angiogenesis targeting ligand, a tumor apoptosis targeting ligand, a disease receptor targeting ligand, amifostine, angiostatin, monoclonal antibody C225, monoclonal antibody CD31, monoclonal antibody CD40, capecitabine, a COX-2 inhibitor, deoxycytidine, fullerene, herceptin, human serum albumin, lactose, leuteinizing hormone, pyridoxal, quinazoline, thalidomide, transferrin, or tri-Me lysine. The present invention also pertains to kits employing the compds. of interest, and methods of assessing the pharmacol. of an agent of interest using the present compds.

L15 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:427503 HCAPLUS Full-text
DOCUMENT NUMBER: 143:301417
TITLE: Regional radiochemotherapy using in situ hydrogel
AUTHOR(S): Azhdarinia, Ali; Yang, David J.; Yu, Dong-Fang; Mendez, Richard; Oh, Changsok; Kohanim, Saady; Bryant, Jerry; Kim, E. Edmund
CORPORATE SOURCE: Division of Diagnostic Imaging, The University of Texas M. D. Anderson Cancer Center, Houston, TX, USA
SOURCE: Pharmaceutical Research (2005), 22(5), 776-783
CODEN: PHREEB; ISSN: 0724-8741
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 20 May 2005
AB To evaluate the feasibility of regional radiochemotherapy of mammary tumors using in situ hydrogel loaded with cisplatin (CDDP) and rhenium-188 (188Re). Sodium alginate (SA) and calcium chloride were used to create a hydrogel for delivery of CDDP and 188Re. In vitro studies were performed to evaluate cytotoxic effects of 188Re-hydrogel and sustained-release ability of the CDDP-hydrogel. Tumor-bearing rats were injected with 188Re-hydrogel (0.5-1 mCi/rat), 188Re-perrhenate (0.5-1 mCi/rat, intratumoral, I.T.), CDDP-hydrogel (3 mg/kg), and 188Re-hydrogel loaded with CDDP (3 mg/kg body weight, 0.5-1 mCi/rat), resp., and groups receiving 188Re were imaged at 24 and 48 h postinjection. Tumor volume, body weight, imaging, and kidney function were assessed as required for each group. Successful formation of the hydrogel was demonstrated by cytotoxic effects of 188Re-hydrogel and slow release of CDDP-hydrogel in vitro. Tumor volume measurements showed significant delay in tumor growth in treated vs. control groups with minimal variation in normal kidney function for the CDDP-hydrogel group. Scintigraphic images indicated localization of 188Re-hydrogel in the tumor site up to 48 h postinjection. Our data demonstrate the feasibility of using hydrogel for delivery of chemotherapeutics and radiation locally. This technique may have applications involving other contrast modalities as well as treatment in cases where tumors are inoperable.
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:283370 HCAPLUS Full-text
DOCUMENT NUMBER: 142:331961
TITLE: Mechanism-based targeted pancreatic beta cell imaging and therapy
INVENTOR(S): Yang, David J.; Oh, Chang-sok ; Kohanim, Saady; Yu, Dong-Fang; Azhdarinia, Ali; Bryant, Jerry
PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005027981	A1	20050331	WO 2004-US30374	200409 16
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004273911	A1	20050331	AU 2004-273911	200409 16
CA 2539384	A1	20050331	CA 2004-2539384	200409 16
US 2005100506	A1	20050512	US 2004-942615	200409 16
EP 1675625	A1	20060705	EP 2004-788800	200409 16
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
BR 2004014512	A	20061107	BR 2004-14512	200409 16
CN 1867363	A	20061122	CN 2004-80030089	200409 16
NO 2006001645	A	20060411	NO 2006-1645	200604 11
PRIORITY APPLN. INFO.:			US 2003-503683P P	200309 17
			WO 2004-US30374 W	200409 16

ED Entered STN: 01 Apr 2005
AB Compns. for imaging beta cells comprise chelator-antidiabetic agent conjugates and optionally chelated metals are described. Examples of agents are 99mTc-DTPA conjugated to nateglinide, glipizide, glyburide or glimepiride.
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:777620 HCAPLUS Full-text
DOCUMENT NUMBER: 142:425977
TITLE: Assessment of Therapeutic Tumor Response Using 99mTc-Ethylenedicysteine-Glucosamine
AUTHOR(S): Yang, David; Yukihiro, Masashi; Yu, Dong-Fang; Ito, Megumi; Oh,

Chang-Sok; Kohanim, Saady; Azhdarinia, Ali; Kim, Chang-Guhn; Bryant, Jerry; Kim, E. Edmund; Podoloff, Donald
CORPORATE SOURCE: Department of Nuclear Medicine, The University of Texas M. D. Anderson Cancer Center, Houston, TX, 1515, USA
SOURCE: Cancer Biotherapy & Radiopharmaceuticals (2004), 19(4), 443-456
CODEN: CBRAFJ; ISSN: 1084-9785
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 24 Sep 2004
AB Purpose: The aim of this study was to evaluate 99mTc- ethylenedicysteine-glucosamine (EC-DG) for the assessment of tumor growth. Method: To evaluate whether 99mTc-EC-DG is involved in cell nuclei activity, in vitro thymidine incorporation, and cell-cycle assays of EC-DG were conducted using lung and breast cancer cells. Biodistribution of 99mTc-EC-DG in lung tumor-bearing mice (0.5-4 h, 1 Ci/mouse, i. v.) was used to estimate the radiation-absorbed dose. Autoradiograms of 99mTc-EC-DG and 18F-FDG were compared in nude mice bearing uterine sarcoma. Rabbits inoculated with VX-2 cells were imaged with 99mTc-EC-DG and 99mTc-EC. For therapeutic assessment studies, scintigraphic imaging studies with 99mTc-EC-DG in mammary tumor-bearing rats were conducted at various days after treatment with paclitaxel and cisplatin. The imaging findings were correlated immunohistochem. assays (mRNA expression, apoptosis, and cell-cycle changes in tumor), and flow cytometry anal. was performed. Results: In vitro cellular uptake assays indicated that cell nuclei activity could be assessed by 99mTc-EC-DG. Scintigraphy and autoradiograms in animal models demonstrated that the tumor could be clearly visualized by 99mTc-EC-DG. The efficacy of paclitaxel and cisplatin treatment in rodent models could be assessed using tumor/muscle ratios. Immunohistochem. staining indicated a reduced expression of bFGF and an increased apoptosis and cell-cycle changes after paclitaxel and cisplatin treatment. Conclusion: 99mTc-EC-DG is involved in cell nuclei activity and could assess the therapeutic tumor response.
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:430988 HCAPLUS Full-text
DOCUMENT NUMBER: 140:419980
TITLE: Ethylenedicysteine (EC)-drug conjugates, compositions and methods for tissue specific disease imaging
INVENTOR(S): Yang, David J.; Yu, Dong-Fang ; Oh, Chang-Sok; Bryant, Jerry L., Jr.
PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA; Cell Point, LLC
SOURCE: PCT Int. Appl., 113 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004044227	A2	20040527	WO 2003-US36078	200311 07
WO 2004044227	A3	20041111		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,				

SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2505537	A1	20040527	CA 2003-2505537	20031107
AU 2003297261	A1	20040603	AU 2003-297261	20031107
US 2004166058	A1	20040826	US 2003-703405	20031107
EP 1562641	A2	20050817	EP 2003-811262	20031107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003016046	A	20050913	BR 2003-16046	20031107
CN 1723042	A	20060118	CN 2003-80105318	20031107
JP 2006515835	T	20060608	JP 2004-552132	20031107
NO 2005002265	A	20050803	NO 2005-2265	20050510
PRIORITY APPLN. INFO.:			US 2002-424493P P	20021107
			WO 2003-US36078 W	20031107

OTHER SOURCE(S): MARPAT 140:419980
ED Entered STN: 27 May 2004
AB The invention provides, in a general sense, a new labeling strategy employing compds. that are N2S2 chelates conjugated to a targeting ligand, wherein the targeting ligand is a disease cell cycle targeting compound, a tumor angiogenesis targeting ligand, a tumor apoptosis targeting ligand, a disease receptor targeting ligand, amifostine, angiostatin, monoclonal antibody C225, monoclonal antibody CD31, monoclonal antibody CD40, capecitabine, COX-2, deoxycytidine, fullerene, herceptin, human serum albumin, lactose, leuteinizing hormone, pyridoxal, quinazoline, thalidomide, transferrin, or tri-Me lysine. The present invention also pertains to kits employing the compds. of interest, and methods of assessing the pharmacol. of an agent of interest using the present compds.

L15 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:371970 HCAPLUS Full-text
DOCUMENT NUMBER: 141:49696
TITLE: Assessment of cyclooxygense-2 expression with 99mTc-labeled celebrex
AUTHOR(S): Yang, David J.; Eryant, Jerry; Chang, Joe Y.; Mendez, Richard; Oh, Chang-Sok; Yu, Dong-Fang; Ito, Megumi; Azhdarinia, Ali; Kohanim, Sahar; Kim, E. Edmund; Lin, Edward; Podoloff, Donald A.
CORPORATE SOURCE: Division of Diagnostic Imaging, University of

Texas M. D. Anderson Cancer Center, Houston, TX, USA
SOURCE: Anti-Cancer Drugs (2004), 15(3), 255-263
CODEN: ANTDEV; ISSN: 0959-4973
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 07 May 2004
AB Cyclooxygenase-2 (COX-2) plays an important role in angiogenesis and cancer progression. Since many tumor cells exhibit COX-2 expression, functional imaging of COX-2 expression using celebrex (CBX, a COX-2 inhibitor) may provide not only a non-invasive, reproducible, quantifiable alternative to biopsies, but it also greatly complements pharmacokinetic studies by correlating clin. responses with biol. effects. Moreover, mol. endpoints of anti-COX-2 therapy could also be assessed effectively. This study aimed at measuring uptake of 99mTc-EC-CBX in COX-2 expression in tumor-bearing animal models. In vitro Western blot anal. and cellular uptake assays were used to examine the feasibility of using 99mTc-EC-CBX to measure COX-2 activity. Tissue distribution studies of 99mTc-EC-CBX were evaluated in tumor-bearing rodents at 0.5-4 h. Dosimetric absorption was then estimated Planar scintigraphy was performed in mice, rats and rabbits bearing tumors. In vitro cellular uptake indicated that cells with higher COX-2 expression (A549 and 13762) had higher uptake of 99mTc-EC-CBX than lower COX-2 expression (H226). In vivo biodistribution of 99mTc-EC-CBX in tumor-bearing rodents showed increased tumor:tissue ratios as a function of time. In vitro and biodistribution studies demonstrated the possibility of using 99mTc-EC-CBX to assess COX-2 expression. Planar images confirmed that the tumors could be visualized with 99mTc-EC-CBX from 0.5 to 4 h in tumor-bearing animal models. We conclude that 99mTc-EC-CBX may be useful to assess tumor COX-2 expression. This may be useful in the future for selecting patients for treatment with anti-COX-2 agents.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:54939 HCAPLUS Full-text
DOCUMENT NUMBER: 139:159553
TITLE: Assessment of epidermal growth factor receptor with 99mTc-ethylenedicysteine-C225 monoclonal antibody
AUTHOR(S): Schechter, Naomi R.; Yang, David J.; Azhdarinia, Ali; Kohanim, Sahar; Wendt, Richard, III; Oh, Chang-Sok; Hu, Mickey; Yu, Dong-Fang; Bryant, Jerry; Ang, K. Kian; Forster, Kenneth M.; Kim, E. Edmund; Podoloff, Donald A.
CORPORATE SOURCE: Div. Radiation Oncology, Univ. Texas, Houston, TX, USA
SOURCE: Anti-Cancer Drugs (2002), Volume Date 2003, 14(1), 49-56
CODEN: ANTDEV; ISSN: 0959-4973
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 23 Jan 2003
AB Epidermal growth factor receptor (EGFR) plays an important role in cell division and cancer progression, as well as angiogenesis and metastasis. Since many tumor cells exhibit the EGFR on their surface, functional imaging of EGFR provides not only a non-invasive, reproducible, quantifiable alternative to biopsies, but it also greatly complements pharmacokinetic studies by correlating clin. responses with biol. effects. Moreover, mol. endpoints of anti-EGFR therapy could be assessed effectively. C225 is a chimeric monoclonal antibody that targets the human extracellular EGFR and inhibits the growth of EGFR-expressing tumor cells. Also, it has been demonstrated that C225, in combination with chemotherapeutic drugs or radiotherapy, is effective in eradicating well-established tumors in nude mice. We have developed 99mTc-labeled C225 using ethylenedicysteine (EC) as a chelator. This study aimed at measuring uptake of 99mTc-EC-C225 in EGFR tumor-bearing animal models and preliminary feasibility of imaging patients with head and neck carcinomas. Western blot anal. and cytotoxicity assays were used to examine the integrity of EC-C225. Tissue distribution studies of 99mTc-EC-

C225 were evaluated in tumor-bearing rodents at 0.5-4 h. biodistribution of 99mTc-EC-C225 in tumor-bearing rodents showed increased tumor-to-tissue ratios as a function of time. and biodistribution studies demonstrated the possibility of using 99mTc-EC-C225 to assess EGFR expression. SPECT images confirmed that the tumors could be visualized with 99mTc-EC-C225 from 0.5 to 4 h in tumor bearing rodents. We conclude that 99mTc-EC-C225 may be useful to assess tumor EGFR expression. This may be useful in the future for selecting patients for treatment with C225.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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